Digitized by the Internet Archive
in 2018 with funding from
University of Toronto

https://archive.org/details/medjournalNov1953uoft

THE UNIVERSITY OF TORONTO
MEDICAL JOURNAL
VOLUME XXXI TORONTO, NOVEMBER 1953 NUMBER 2

THE SYNDROMES ACCOMPANYING CEREBRAL ARTERIAL INFARCTION

H. H. HYLAND AND D. LEVY*

Cerebral infarction resulting from occlusion of cerebral arteries may be caused by thrombosis superimposed on atheromatous change in a vessel, or by embolism. The distinction between thrombosis and embolism is usually made clincially by the presence or absence of a source for embolism such as recent cardiac infarction, auricular fibrillation or subacute bacterial endocarditis. In a proportion of cases, particularly those with small areas of softening, no pathological evidence of thrombosis or embolism may be found. In such cases arteriolar spasm or, where severe arteriolar sclerosis exists, a relative ischaemia associated with fluctuations in blood pressure are possible mechanisms.

The study of patients with arterial infarction has added greatly to our knowledge of cerebral function. These lesions are discrete, usually causing relatively little disturbance of function remote from the area affected, thus often permitting accurate clinical localization. Other disease entities affecting the brain such as hemorrhage and tumour tend to produce remote effects due to their expanding nature which may result in a less clearly defined clinical representation of the actual site of the lesion.

Cerebral thrombosis is the commonest cerebrovascular lesion. In most instances the condition becomes manifest when the patient is at rest in contrast to cerebral hemorrhage, which may occur at any time but most frequently during activity. With thrombosis the clinical manifestations usually reach a maximum in a matter of minutes or hours although brief premonitory sensations are sometimes present intermittently for days or weeks previously. With embolism the onset is sudden and recovery is likely to be much more rapid and complete than occurs with thrombosis. Gradually progressing symptoms developing over days or weeks are unlikely to be a result of arterial occlusion and such cases usually turn out to have an expanding lesion as the basis.

*From the Department of Medicine, University of Toronto, and the Medical Service of the Toronto General Hospital.

The purpose of this article is to describe the significant anatomical features and the clinical syndromes that are encountered with occlusion of the various cerebral arteries.

Internal Carotid Artery

The internal carotid artery supplies the anterior part of the brain, the eye and its appendages and sends branches to the forehead and nose. The artery begins at the bifurcation of the common carotid opposite the upper border of the thyroid cartilage and runs upward in front of the tranverse processes of the upper 3 cervical vertebrae to the carotid canal in the petrous portion of the temporal bone. Its petrous course is characterized by considerable curving of the vessel and it leaves the canal to enter the cavity of the skull at the side of the body of the sphenoid bone. Here it is situated between the layers of the dura mater forming the cavernous sinus. It curves upwards to the medial side of the anterior clinoid process to perforate the dura forming the roof of the cavernous sinus where it gives off the ophthalmic artery (Fig. 1). It then passes between the optic and oculomotor nerves to the anterior perforated substance where it gives off its terminal branches: the posterior communicating, anterior choroidal, anterior cerebral and middle cerebral arteries.

It is only recently that thrombosis of the extracranial portion of the internal carotid artery has been recognized as a not uncommon occurrence. In the past it has often been missed because this part of the vessel is used for embalming the head and consequently it has not been regularly examined at autopsy. Studies have shown that the region of the carotid sinus is a point of special selection for the occurrence of atherosclerosis (Fig. 2) and well marked

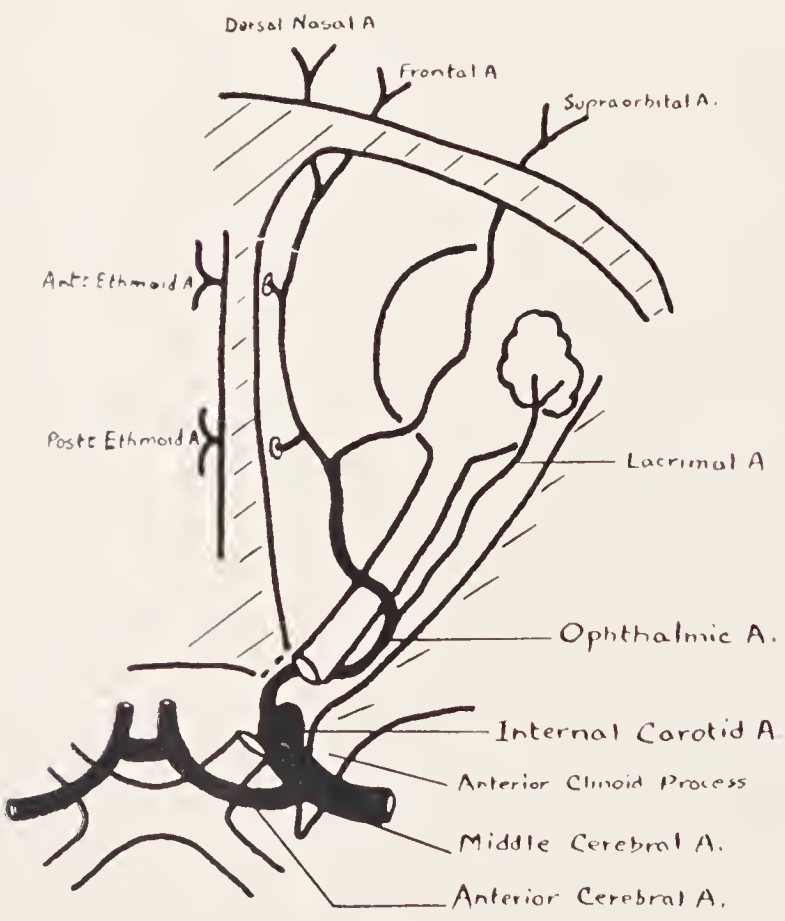


Fig. 1. Diagram to show terminal branching of the internal carotid artery.

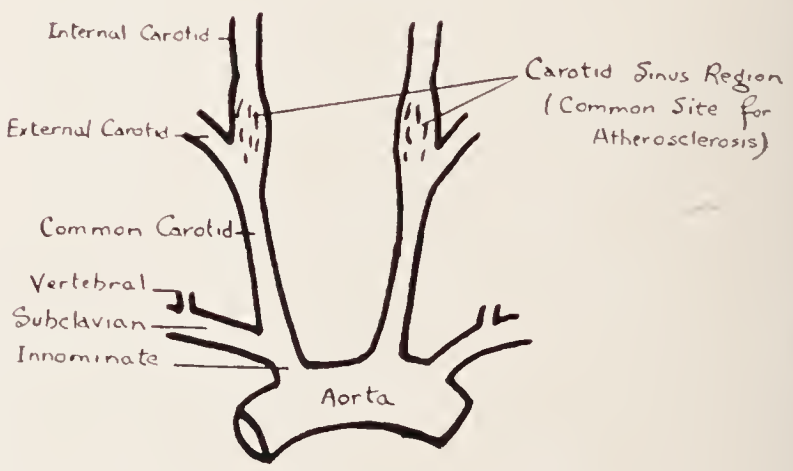


Fig. 2. Diagram showing the commencement of the internal carotid artery.

changes have been found at this site in comparatively young patients. Increased narrowing of the lumen precedes the final occlusion which occurs due to superimposed thrombosis. The extent of the brain damage following occlusion is a measure of the adequacy of the anastomotic circulation in the circle of Willis

(Fig. 3). Anomalies of the vessels comprising the circle of Willis are common (Fig. 8) and they may render the collateral circulation inadequate thus determining the occurrence of symptoms when one internal carotid artery is partially or completely occluded. This lesion may explain some of the cases of infarction found in the distribution of the anterior and middle cerebral arteries where autopsy has failed to reveal thrombosis in these vessels to account for it.[1]

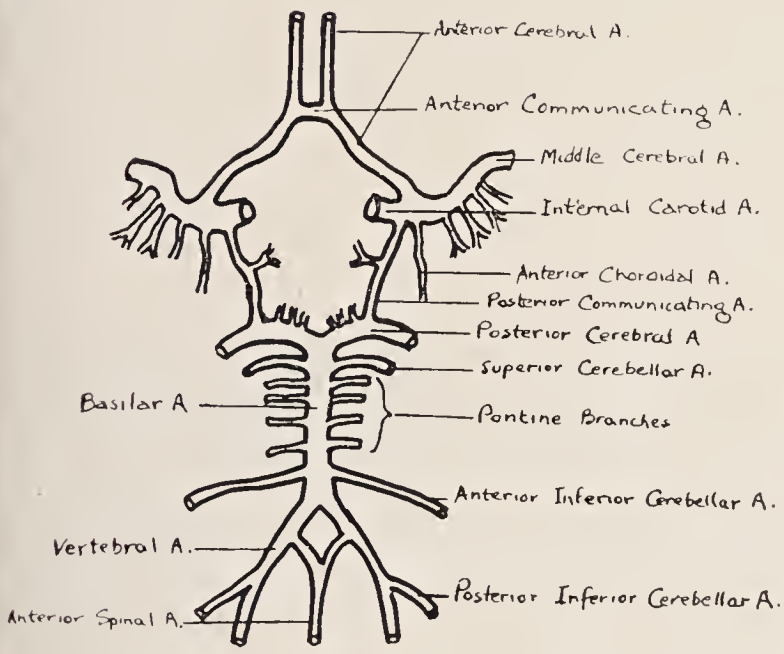


FIG. 3. Diagram of the arteries at the base of the brain.

Most commonly the clinical picture is a severe hemiplegia on the opposite side preceded by periodic unilateral weakness or paresthesia with or without visual impairment in the homolateral eye, attacks of dizziness or unconsciousness and, if the lesion is left-sided, aphasia. All or some of these symptoms may occur intermittently over days, weeks or months and they are produced by a recurring relative ischaemia in the distribution of the terminal branches of the internal carotid artery. Attacks of homolateral headache resembling migraine have been described. It has been postulated that vasoconstriction in the terminal branches of the artery is responsible for the transient phenomena and possibly also for the final hemiplegia in some cases, since a clinical picture identical with occlusion of the internal carotid artery can occur and yet a channel be shown to exist by arteriogram.[2]

Gradual occlusion of one or both carotid arteries may cause a progressive picture of senile dementia with or without hemiplegias, the symptoms being due to gradual cerebral ischemia.[3]

Occlusion of the extracranial portion of the internal carotid artery may often be recognized during the acute phase of hemiplegia by the absence or diminution of the carotid pulsation high in the neck and it can be confirmed by arteriography although this procedure is not without danger in elderly persons.

Case I. A 60-year-old man noted clumsiness and numbness of the left hand while at work on Dec. 4th, 1951. This cleared up entirely after a few days but one month later he began to experience numbness and tingling in the left hand and around the left side of the mouth occurring in brief attacks. Two weeks later he developed persistent weakness of the left hand and some difficulty in walking.

On examination he was mentally dull. There was a bruit heard over both eyes and over the left common carotid artery. He had a left attention hemianopia, slight left lower facial weakness and some weakness and mild spasticity in the left upper and lower limbs. Astereognosis of the left hand was present. During observation in hospital the findings showed some variation from day to day.

Right and left carotid arteriograms were done. On the right side only the stump of the internal carotid artery was

filled (Fig. 4). Injection of the left side revealed excellent filling of the left internal carotid and its branches and the dye had passed across the circle of Willis to enter the right middle and anterior cerebral arteries (Fig. 5). The findings by arteriogram provided conclusive evidence that the right internal carotid artery had been occluded.

Occlusion of the intracranial portion of the internal carotid artery causes a hemiplegia on the opposite side which is likely to be sudden in onset accompanied by blindness on the homolateral side due to deprivation of circulation in the ophthalmic branch of the artery. In such cases the carotid pulsation in the neck is not likely to be affected.

Anterior Choroidal Artery

This vessel usually arises from the internal carotid just before it bifurcates into the anterior and middle cerebral arteries (Fig. 3) but sometimes it arises from the middle cerebral at its commencement. The artery swings laterally to enter the substance of the brain in the angle between the cerebral peduncle and the temporal lobe. It supplies the uncus, the optic tract, the middle third of the cerebral peduncle, most of the globus pallidus, the posterior two-thirds of the inferior half of the posterior limb of the internal capsule (Fig. 6), the anterior half of the subthalamic nucleus, the red nucleus and the lateral aspect of the external geniculate body.

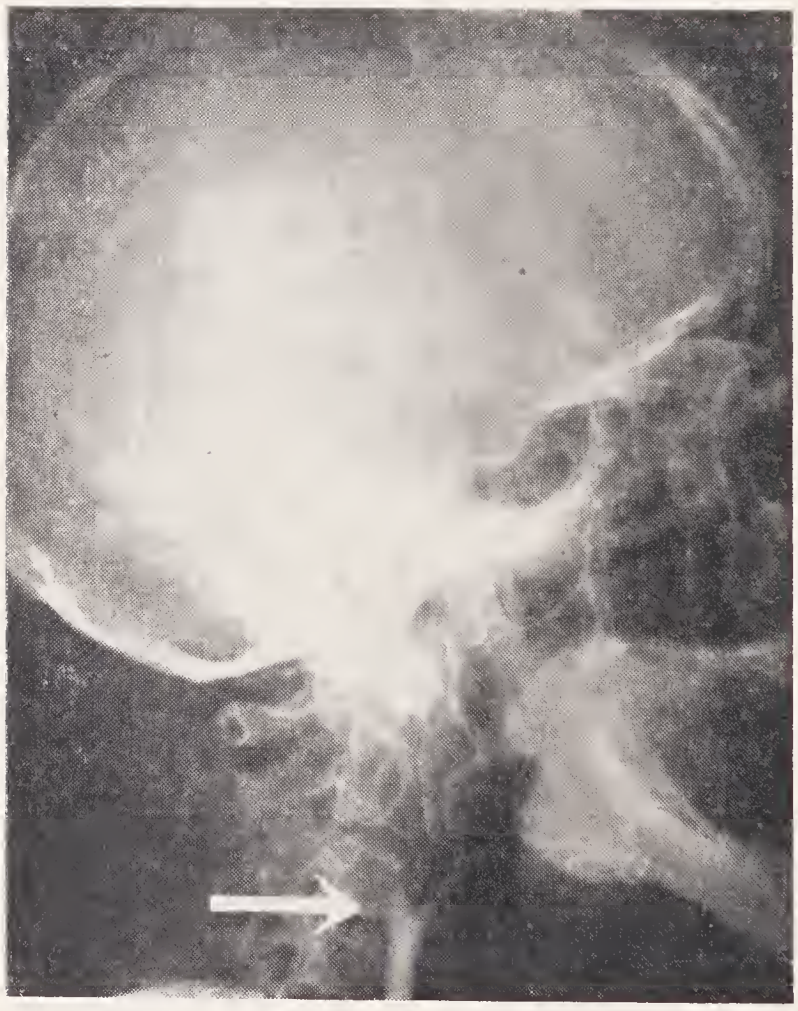


Fig. 4. Case I. Lateral view of skull after injection of the right common carotid artery with diodrast. It will be seen that the external carotid is well outlined but the dye has not extended beyond the commencement of the right internal carotid artery.

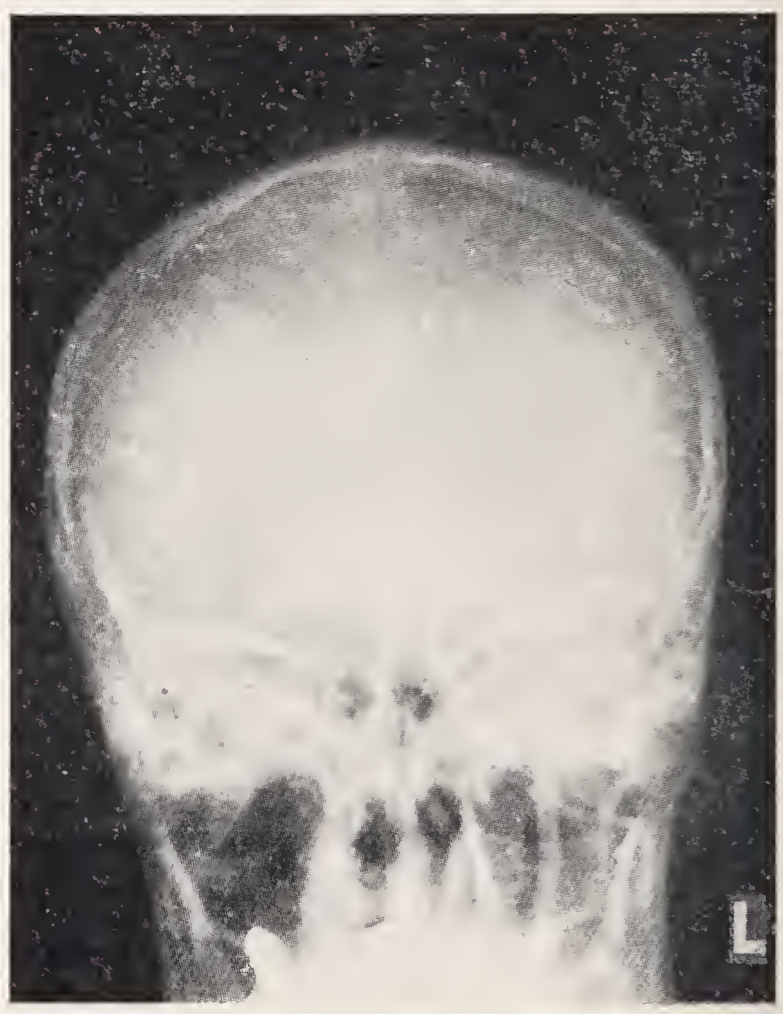


Fig. 5. Case I. Anteroposterior view of skull after injection of diodrast into the left common carotid artery showing the dye in the left internal carotid artery and that it has passed across the circle of Willis to enter the cerebral arteries on the right side.

There are few verified cases of occlusion of this artery in the literature. It is considered that there will result a contralateral hemiplegia, hemianaesthesia and hemianopia without loss of consciousness. However Cooper[4] in a recent report describes 8 cases where surgical ligation of this vessel had been done for intractable involuntary movements. There were no instances of hemiplegia or hemianesthesia and no hemianopia on confrontation testing in any of these cases.

Anterior Cerebral Artery

This is one of the terminal branches of the internal carotid. The vessel runs anteromedially between the medial olfactory stria and the optic nerve towards the longitudinal cerebral fissure. At the margin bordering the mesial and orbital surfaces of the hemispheres the two anterior cerebral arteries are joined together by the anterior communicating artery. The anterior cerebral then abruptly changes its course and turns upward over the genu of the corpus cal-

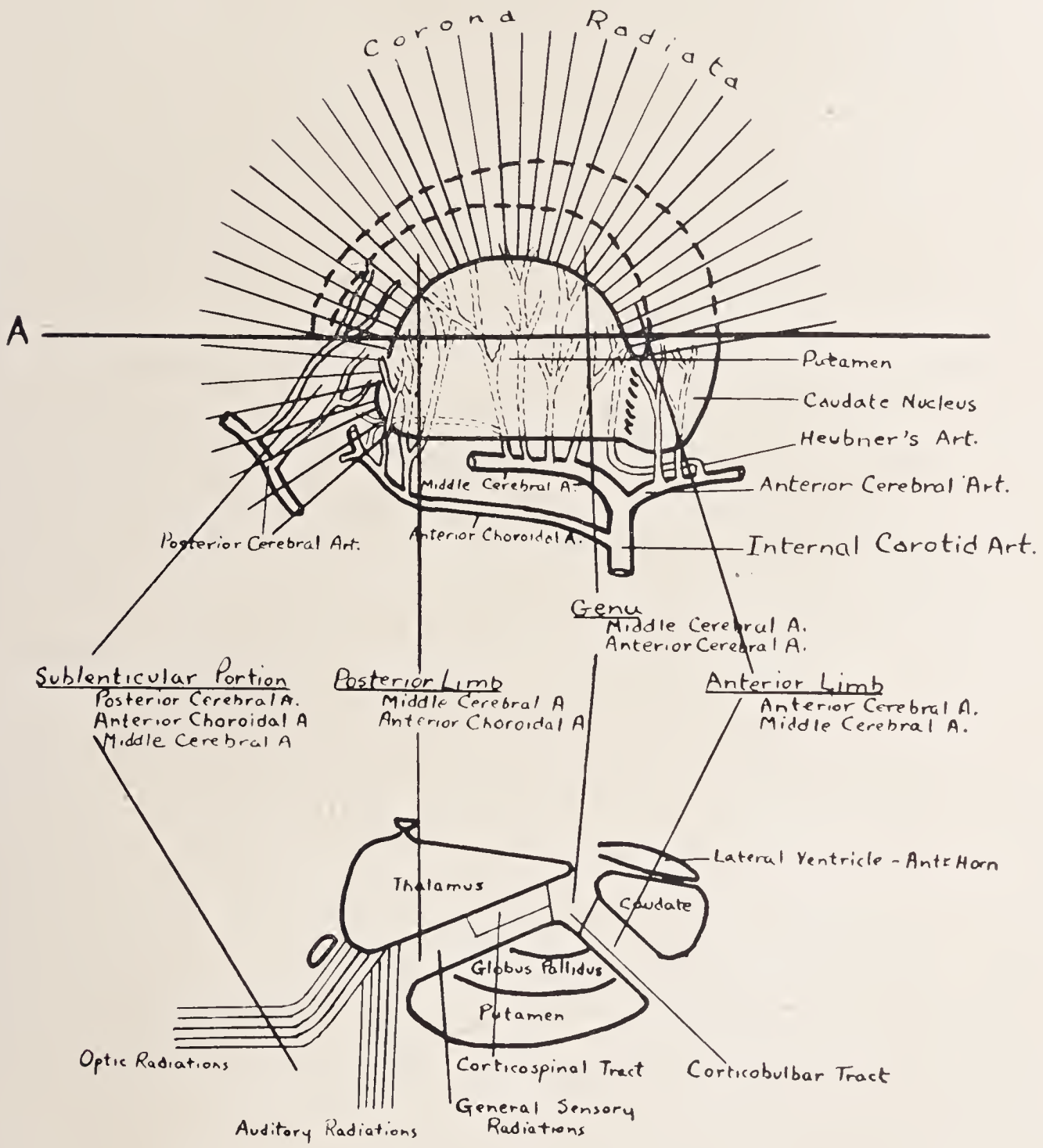


FIG. 6. Diagram to show origin of arterial supply to internal capsule *Above*: Lateral view showing the arteries and their region of supply. *Below*: Horizontal section at level A.

losum and finally pursues a horizontal course along the body of the corpus callosum. It ends usually at the parieto-occipital fissure (Fig. 7).

pallidus. One of these, "Heubner's" artery, supplies in addition the anterior limb of the internal capsule (Fig. 6). The branches from the upper surface of

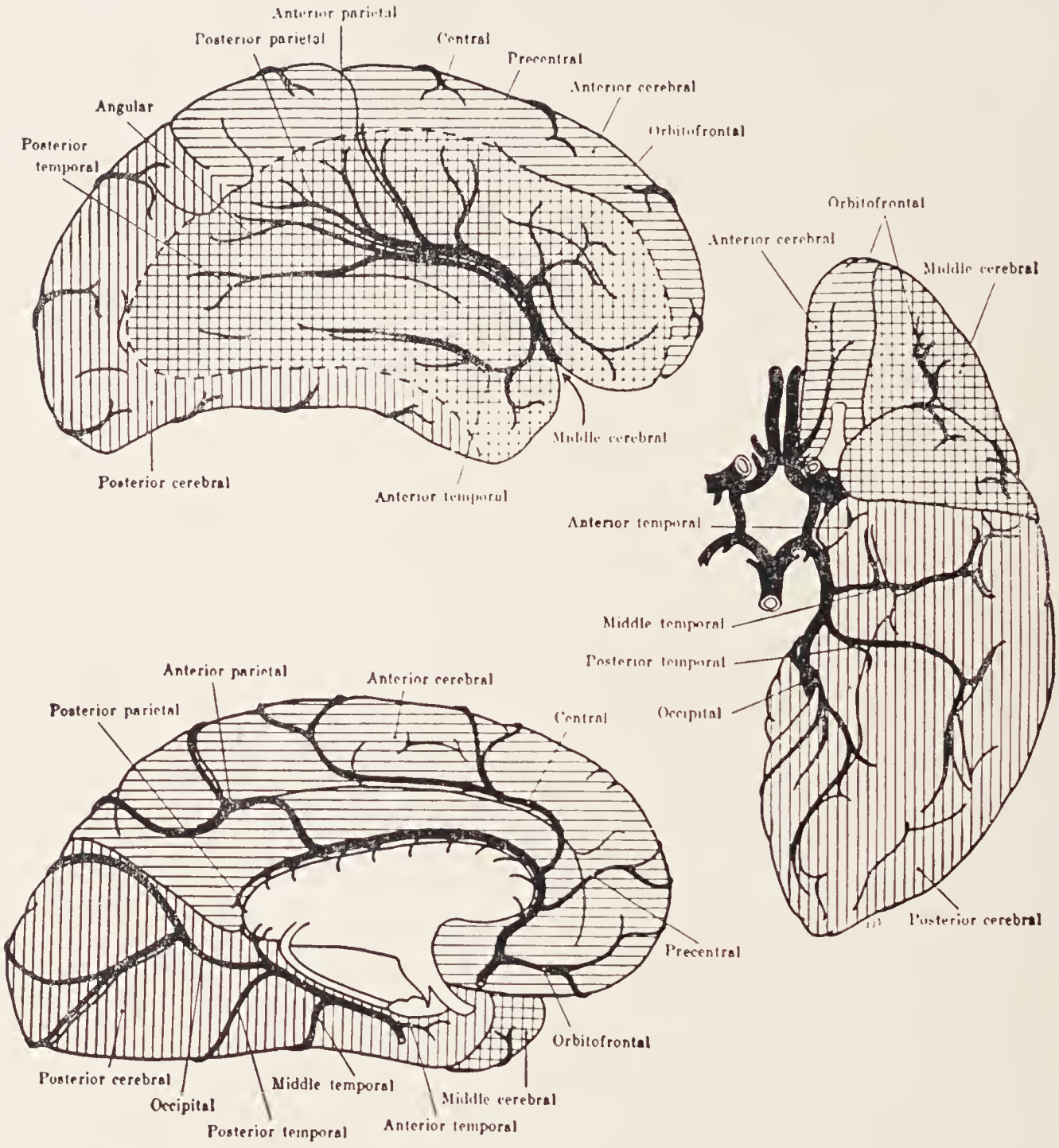


FIG. 7. (From Mettler) Diagram of areas of brain supplied by the superficial branches of the three main cerebral arteries.

The branches include the basal, the anterior communicating artery, the branches from the upper surface and the branches from the under surface of each artery. The basal branches enter the anterior perforated spot and are distributed to the ventral portions of the heads of the caudate nucleus and of the putamen as well as to the frontal pole of the globus

the artery supply the whole of the mesial surfaces of the frontal and parietal lobes and the white matter subjoining it to a depth of 2.5 cms. The branches going off the under surface of the horizontal portion of the artery supply the genu and anterior four-fifths of the corpus callosum.

The most important function of the

anterior cerebral artery is to supply that portion of the motor cortex subserving leg movements.

Total occlusion of an anterior cerebral artery will include involvement of Heubner's branch and there will be softening in the whole area of distribution of the vessel. The result is a hemiplegia of severe degree with sensory loss in the paralysed leg, some degree of aphasia if the lesion is left-sided, mental change and impairment of bladder sphincter control.[5] The hemiplegia is due to the effect on the anterior part of the internal capsule (Heubner's artery) as well as to involvement of the paracentral lobule. The former lesion causes paralysis of the face, tongue and upper extremity, particularly its proximal portion, and the latter marked weakness in the lower extremity. The sensory impairment in the lower limb is due to the involvement of the mesial portion of the post central convolution. Urinary incontinence often occurs due to the lesion affecting the paracentral lobule where the cortical representation for the bladder is situated. If aphasia is present it is of the expressive type and temporary. It is a result of involvement of the subcortical white matter beneath Broca's area, which is supplied by Heubner's artery. Mental changes include retardation, confusion and disorientation.

Occlusion distal to Heubner's artery results in hemiplegia with predominant involvement of the leg, mild involvement of the upper limb and rarely any evidence of facial weaknes. There is usually sensory impairment on the leg and temporary loss of sphincter control. There may be some mental impairment and also transient aphasia if the lesion is left-sided. Forced grasping and groping of the affected hand is commonly present due to the involvement of the posterior part of the superior frontal convolution. Left-sided ideomotor apraxia occurs in many cases regardless of the side of the lesion. It is due to softening of the corpus callosum. In right-handed persons the region of the brain determining the formulation of the idea of an act and the development of its pattern is in the lower and posterior part of the left parietal lobe in the region of the supramarginal gyrus. The connections from the left supramarginal gyrus to the right motor cortex pass by way of the corpus callosum and therefore apraxia is unilateral and left-sided regardless of which anterior cerebral artery is occluded. It is only when the region of the supramarginal gyrus in the left parietal lobe is injured specifically that apractic symptoms are bilateral. Ideomotor apraxia is shown by the patient's inability to carry out previously learned actions on command such as to salute, blow a kiss, etc., despite the presence of adequate power in the limbs. When the thrombosis is in the right anterior cerebral trunk at the point of emergence of Heubner's artery the resulting severe hemiplegia obscures the apraxia.

Bilateral thrombosis of the anterior cerebral arteries is occasionally seen and is usually due to an anomalous formation whereby only one anterior cerebral artery is present forming a common trunk for the supply of both hemispheres. The following case, previously reported,[6] will be cited briefly since it illustrates so well the symptoms that occur with occlusion of this vessel.

Case II. A scrubwoman, age 61, 5 days before admission to the hospital collapsed while working. She experienced no loss of consciousness, but was unable to stand. Three days later she com-

plained of weakness in the left arm. On admission, she was euphoric and loquacious and at times became vulgar and profane. Attention was poor, but there was no gross mental confusion. The left leg was completely paralysed; the left arm was partially paralysed, with apraxia and a grasp reflex present. The right arm and leg were in a constant state of motor activity, the right hand grasping objects within reach but releasing them on command. A few days later she became aphasic; the right arm and leg were totally paralysed; the left arm moved constantly, groping and grasping at objects. There was some return of power in the left leg. Both plantar reflexes were in extension. Subsequently the patient became comatose, and all movement in the limbs ceased. Death occurred on the 12th day after the onset.

Autopsy revealed several anomalies of the vessels of the circle of Willis including an anomalous distribution of the anterior cerebral arteries (Fig. 8). There was no anterior communicating artery and the two vessels united to form one long stem which subsequently divided into two on the dorsum of the corpus callosum (Fig. 9). A thrombus was pres-

FIG. 8. Case II. Drawing of the circle of Willis to show the anomaly of the anterior cerebral arteries and the various other arterial anomalies that existed.

FIG. 9. Case II. The small right anterior cerebral artery is seen uniting with the vessel on the left side to form a common trunk in which thrombosis occurred.

ent in the common trunk and softening was found in the anterior cerebral distribution of both hemispheres.

The above case with occlusion of an anomalous vessel is, of course, unusual but occlusion of one anterior cerebral artery is not uncommon. The following case, recently observed in hospital, will be described briefly.

Case III. A woman, aged 67 years, known to be hypertensive, had symptoms of arteriosclerotic heart disease for 10 years. On the day of admission to hospital she collapsed on the bathroom floor without loss of consciousness. On examination the left leg was totally powerless and there was some weakness of the left upper limb. There was no facial weakness. The tendon reflexes were increased in the left upper and lower limbs and the plantar response was dorsiflexion. The patient showed a grasp reflex in the left hand and was incontinent of urine. The diagnosis was thrombosis of the right anterior cerebral artery. She made a gradual recovery over the next few weeks. The function of the left leg improved so that she could walk without assistance. The grasp reflex subsided and she regained normal use of the left upper limb. The incontinence cleared up completely.

Middle Cerebral Artery

Each of these vessels moves laterally across the anterior perforated substance to enter the Sylvian fissure where they divide into terminal branches distributed to the insula and the lateral surface of each cerebral hemisphere.

As the middle cerebral artery crosses the anterior perforated substance it gives rise to a number of ganglionic branches of varying sizes which enter the brain to supply most of the putamen, large parts of the globus pallidus and caudate nucleus as well as the whole of the internal capsule above the level of the globus pallidus (Fig. 6). As the vessel traverses the Sylvian fissure it gives off its cortical branches including the orbitofrontal, precentral, anterior parietal, posterior parietal, angular, posterior temporal and the anterior temporal arteries (Fig. 7).

Occlusion of the main trunk of a middle cerebral artery causes softening of a large portion of the cerebral hemisphere and results in a contralateral hemiplegia, hemianesthesia and hemianopia with deviation of the head and eyes away from the lesion at first and later towards the side of the lesion. The hemianopia is due to involvement of the "deep optic branch" of the middle cerebral artery which supplies the auditory and optic radiations immediately after they leave the capsule.[7] If the patient survives, the hemianopia may disappear after the first few weeks unless the anterior choroidal artery has arisen from the middle cerebral, as it sometimes does, and has been included in the occlusion. If the lesion is on the side of the dominant hemisphere global aphasia is present. Unlike the hemiplegia that follows occlusion of the anterior cerebral artery, the paralysis of the face and arm is more complete than that of the leg.

When individual branches are occluded only parts of the syndrome appear. Although small areas of softening in the distribution of the middle cerebral are more common with any other artery, clear-cut syndromes resulting from occlusion of the branches are not consistently found. These branches show considerable variation in their distribution and also it is not unusual for more than one to be involved because of the gen-

eralized arterial disease that exists in such patients.

Occlusion of one or more of the ganglionic branches of the middle cerebral causes softening of variable extent in the internal capsule, the usual manifestations being a contralateral hemiplegia with often a mild hemianesthesia and temporary dysarthria. Occlusion of the posterior temporal branch is likely to involve the upper part of the optic radiation and result in a contralateral inferior quadrantic hemianopia. If this lesion occurs in the dominant hemisphere it may cause an aphasia, predominantly receptive. Occlusion of the orbito-frontal branch on the dominant side is accompanied by a predominantly expressive aphasia. Occlusion of the ascending precentral branch gives rise to a contralateral hemiparesis involving mainly the face and upper limb. Softening in the distribution of the posterior parietal branch on the dominant side gives rise to bilateral ideomotor apraxia due to destruction of the supramarginal gyrus. Lesions involving this region in either parietal lobe may cause defects in appreciation of the body image so that if there is a hemiplegia as well, the patient will neglect the hemiplegic limbs and may even deny the existence of the hemiplegia. Occlusion of the angular branch on the dominant side is likely to cause a predominantly receptive aphasia characterized by an impaired ability to appreciate written speech with which may be associated agraphia, acalculia and finger agnosia (Gertsmann's syndrome).

In the following case there were 3 areas of infarction in the brain which are in the distribution of the middle cerebral arteries.

Case IV. A 58-year-old woman, known to be hypertensive for years, had a right-sided stroke 2 years before admission. She evidently made a good recovery and there was little residual disability but since that time she was said to be depressed with a poor memory. The day of admission she had collapsed in her home without loss of consciousness. On admission there was no obvious weakness but she had some increased tone with increased reflexes in the right leg and a dorsiflexion plantar response. She lapsed into coma soon after admission and investigation showed her to have severe diabetes. On treatment the diabetes was controlled but she failed to regain consciousness. Five days after admission she developed conjugate deviation of the eyes to the right. Examination showed spasticity of the left arm and leg and bilateral upgoing toes with decreased response to pin-prick on the left side. Her condition deteriorated with signs of cardiac failure and death ensued.

At autopsy the arteries at the base of the brain showed considerable atherosclerotic thickening with severe narrowing of the lumen of both middle cerebral arteries. There was oedematous swelling of the right hemisphere. On horizontal section the anterior limb and genu of the right internal capsule showed an area of palpable recent softening corresponding with the patient's recent left hemiplegia (Fig. 10). In the anterior limb of the left internal capsule there was a small area of old cystic softening, encroaching slightly on the outer surface of the head of the caudate nucleus. This probably accounts for the "stroke" which occurred 2 years before death. Old softening was also found in the cortical tissue and white matter of the right posterior parietal lobe with cystic degeneration in the subcortical white matter. It is uncertain when

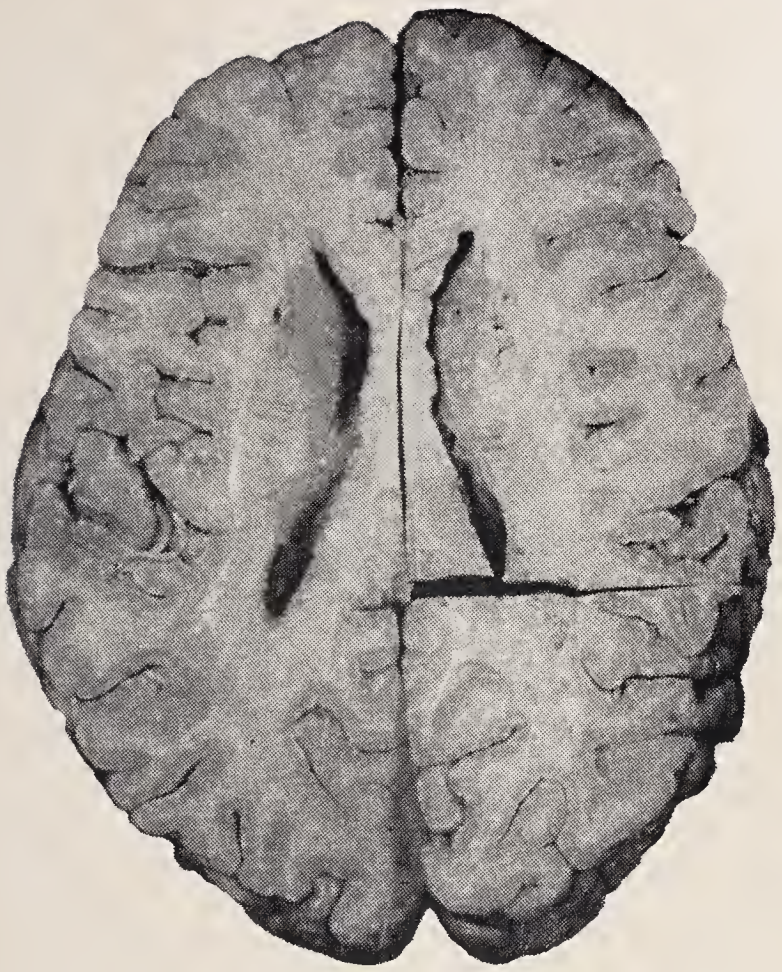


FIG. 10. Case IV. Horizontal section of the brain showing recent softening in the region of the right internal capsule. In the anterior limb of the left internal capsule and in the right posterior parietal lobe old areas of softening are seen.

this latter vascular accident took place but its pathological appearance indicates it to be of long standing. It appears to be in the distribution of the angular branch of the right middle cerebral artery.

Posterior Cerebral Artery

The two posterior cerebral arteries are formed by the division of the basilar at the anterior end of the pons. They pass back between the upper surface of the cerebellum and the under surface of the hemispheres to be distributed to the posterior part of the brain. From the most proximal part of this artery a number of branches are given off which pass into the substance of the cerebral peduncle and the interpeduncular space. In conjunction with similar branches from the posterior communicating artery these supply the red nucleus, the subthalamic region, the mammillary bodies, the cerebral peduncles and the antero medial portion of the thalamus. More distally the posterior cerebral gives off a number of thalamo-geniculate branches which supply the postero-lateral portion of the thalamus, the anterior portion of the pulvinar and contiguous parts of the geniculate bodies.[8] Lateral branches of the artery pass to the adjacent cerebral cortex supplying the medial and inferior surface of the temporal lobe and the occipital lobe as the anterior, middle and posterior temporal branches and the occipital artery, the latter supplying the visual cortex (Fig. 7).

Because of the rich collateral circulation by way of the circle of Willis it is rare for the main trunk of a posterior cerebral artery to be occluded. If a main trunk is thrombosed the area of destruction includes both the thalamus and the visual pathways. The result will be a contralateral hemianopia which may be accompanied by the "thalamic syndrome" of Dejerine-Roussy, namely fleeting contralateral hemiparesis of the flaccid type, severe impairment of superficial and deep sensation often relatively sparing the face with later some recovery of superficial sensation. The recovered sensation is of a peculiar type characterized by elevation of the threshold to cutaneous, thermal and painful stimuli which when perceived have an abnormal painful quality. Associated with this sensory disturbance there is likely to be also intolerable, spontaneous pains of an agonizing, burning quality in the affected limbs. The most reasonable explanation of the hyperpathia is that suggested by L'hermitte:[9] He assumes that the thalamus normally modulates sensory impulses

and that its involvement allows these sensory impulses to reach the cortex without that modulating influence. The affected limbs may show also atrophy, tremor and/or choreoathetoid movements due perhaps to the sensory deficit and to involvement of the subthalamic nuclei and their connections. With left-sided lesions alexia and disturbance in visual orientation may be present.

Thrombosis of the small interpeduncular branches of the posterior cerebral artery occurring without any interference with the main supply of the vessel is rare but the resulting necrosis of the subthalamic region might cause chorea, athetosis or hemibalismus as the sole findings.

Occasionally the thalamogeniculate branches are alone involved and a "thalamic syndrome" could be the only manifestation. Much more commonly however the lesion is confined to the distribution of the occipital and temporal branches and the principal clinical manifestation is a homonymous or a quadrantic hemianopia. The following case illustrates this not uncommon vascular accident very well.

Case V. This 65-year-old man was a long-standing diabetic with hypertension. Ten months before death he awakened one morning with blurred vision. Examination at that time is said to have shown a right homonymous hemianopia, some sensory loss in the right upper limb and a right upgoing toe. The right homonymous hemianopia remained constant. On the morning of admission he was found unconscious in bed with stertorous breathing. There was evidence of cardiac failure. The pupils were pin-point and there was some spasticity of the right arm and leg with bilateral upgoing toes. He died 6 hours after admission.

At autopsy the basal arteries showed moderate arteriosclerotic thickening. The left posterior cerebral artery immediately distal to its origin was markedly narrowed by severe intimal thickening but was still patent. The cortex and white matter on the mesial surface of the left occipital lobe and inferior surface of the left temporal lobe had been completely destroyed (Figs. 11 and 12). The microscopic appearance of the softening was compatible with a lesion 10 months old. Some of the small cortical vessels in the softened area were occluded by organized thrombus.

The basilar artery showed severe arteriosclerosis and narrowing of the lumen. The central pontine tissue was slightly soft on palpation and micro-

FIG. 11. Case V. Mesial surface of brain showing old softening of the left occipital lobe in distribution of the posterior cerebral artery.

scopically there were irregular cystic lesions indicating diffuse softening. This pontine softening, due to partial occlusion of the basilar artery, was evidently a factor in his terminal illness.

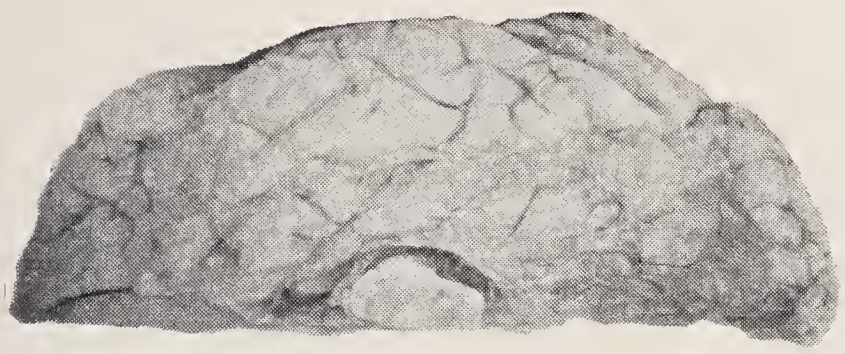


FIG. 12. Case V. Inferior view of the hemisphere shown in Fig. 11 to indicate extent of the softening involving the inferior surface of the left temporal lobe.

BASILAR ARTERY

This vessel is formed by the union of the two vertebral arteries at the lower end of the pons (Fig. 3). The artery runs along the ventral surface of the pons and at the lower end of the midbrain it divides into the two posterior cerebral arteries. Each of these is connected with the remainder of the circle of Willis by a posterior communicating artery which joins the internal carotid artery. The blood supply of the pons is derived entirely from the basilar artery which also contributes some supply to the midbrain, medulla and cerebellum through certain of its branches. However most of the blood supply to the midbrain is derived from the posterior cerebral and the posterior communicating arteries and the medulla is supplied mainly by the vertebral arteries and their branches.

The branches of the basilar can be divided into 3 groups:

1. Paramedian. Three to five of these branches arise on each side from the posterior surface of the basilar, entering the pons laterally to the midline where they branch into small arteries running perpendicularly to the long axis of the pons and supplying the main tracts which lie in the ventro-medial part.

2. Short circumferencial. Four or five of these vessels arise on each side from the lateral wall of the basilar and supply the lateral 3/5 of the pons consisting mostly of tegmentum.

3. Long circumferencial. These comprise the two superior cerebellar arteries and the two anterior inferior cerebellar arteries. The superior cerebellar arteries course around the brain-stem to enter the cerebellum where they supply the superior parts of the hemispheres. In the pons they supply the brachium conjunctivum, the upper part of the brachium pontis and the lateral tegmentum of the pons including the spinothalamic tracts. From the most proximal portions of these vessels small branches are given off which contribute to the blood supply of the midbrain. The anterior inferior cerebellar arteries likewise course around the brain-stem to enter the cerebellar hemispheres supplying the anterior part of the under surface of the cerebellum. In the brain-stem they supply the restiform bodies and the lateral tegmentum of the upper medulla and lower pons including the spinal nuclei and tracts of the fifth nerves and the cochlear and facial nuclei.

When occlusion of the basilar artery occurs by thrombosis or embolus a variety of symptom complexes may occur depending on the position and extent of the occlusion, which in turn determines the form and size of the infarct. For this reason the symptoms and clinical findings often vary from case to case. Thus if the posterior communicating arteries are of good size permitting ample circulation to get back from the anterior part of the circle of Willis a thrombus

limited to a part of the basilar artery would only affect the circulation of the branches actually blocked off. If however the thrombus extends into the posterior cerebral arteries the branches to the thalamus, peduncles and third nerve nuclei will be affected. As a rule when occlusion spreads beyond the junction of the posterior cerebral and posterior communicating arteries infarction of the posterior and inferior parts of the temporal lobe and the occipital lobe will occur as well as the damage to the pons and midbrain.

In spite of the variation in clinical manifestations, the condition is usually easy to recognize. The onset is frequently sudden with unconsciousness, or, if consciousness is retained complaints of headache, dizziness, unilateral paresthesias and mental confusion are often present. Common findings are difficulty in articulation and swallowing which are pseudobulbar in nature, being due to involvement of the corticobulbar pathways in the upper pons. Pupillary abnormalities are likewise common. The pupils may be small and fixed or unequal and fixed. Ocular palsies, most commonly 6th nerve but also 3rd nerve in origin may occur. Hemiplegia is a consistent finding and sometimes alternating hemiplegias are seen. Not infrequently there are crossed hemiplegias with cranial nerve palsies on the side opposite the hemiplegia. With severe lesions a quadriplegia is characteristic and bilateral dorsiflexion plantar responses are a consistent finding. Hemianopia will be present if the thrombosis extends to a posterior cerebral artery beyond the junction with the posterior communicating artery and blindness occurs if both posterior cerebrals become occluded. Hyperpyrexia and changes in respiratory function including tachypnea may be found as terminal signs.

It is of interest that temporary improvement may take place after the onset. Usually however death occurs in a period of from 2 days to 5 weeks after the onset although occasionally patients may survive when the occlusion is partial and limited in extent.

Case VI. This 45-year-old woman was found unconscious in bed on the morning of admission. There was a history of complaints of abdominal pain for 6 days. Examination showed stertorous breathing, pulse rapid and feeble, blood pressure 150/90. The eyes were in the midline. The pupils were large, unequal and did not react to light. The left corneal reflex was diminished and there was a right lower facial weakness. All four limbs were immobile and flaccid. The left leg and right arm responded by

FIG. 13. Case VI. Inferior surface of the brain showing the thrombus in the basilar artery extending into the left vertebral and the proximal portion of the right posterior cerebral artery.

movement to stimuli, the other limbs did not respond. The ankle jerks were absent. The other tendon reflexes were present and showed little difference on the two sides. Both plantar responses were dorsiflexion. The cerebrospinal fluid was normal. Death ensued a few hours after admission.

Autopsy showed a thrombus extending from the left vertebral artery through the basilar to involve the proximal portion of the right posterior cerebral artery (Fig. 13). There was softening of the pons, the right occipital lobe and the hypothalamic region and thalamus on the right side.

BRANCHES OF THE BASILAR. A superior cerebellar artery is rarely occluded alone. If so the signs are likely to include ipsilateral cerebellar deficit due to involvement of the brachium conjunctivum and of the dentate nucleus both of which are supplied by the vessel together with loss of pain and temperature sense on the opposite side of the body including the face, due to interruption of the spinobulbo-thalamic tract in the lateral region of the pons.

An anterior inferior cerebellar artery is likewise rarely the site of a primary thrombosis. The signs would include cerebellar deficit, deafness, facial paralysis and loss of sensation over the face on the side of the lesion with perhaps incomplete loss of pain and temperature sense on the contralateral side of the body.

The paramedian branches of the basilar may be involved alone, in which event the cerebral peduncles are affected and varying degrees of pyramidal tract disease, usually bilateral, are likely to be the predominant finding. There may be also loss of postural sensibility on one or both sides if the fillet is involved and sometimes an ipsilateral external rectus palsy or loss of conjugate deviation of the eyes to the side of the lesion.

Vertebral Artery

This vessel arises from the subclavian artery of each side and ascends through the foramina of the transverse processes of the upper 6 cervical vertebral. It enters the skull through the foramen magnum lying on the ventral surface of the medulla. Here the branches include the posterior inferior cerebellar artery and a number of small paramedian branches which enter the medulla directly. At the lower border of the pons the two vertebral arteries unite to become the basilar but just before this takes place a branch from each vessel goes to form the anterior spinal artery. (Fig. 3)

When cases of thrombosis of the basilar or posterior inferior cerebellar arteries come to autopsy it is common to find the thrombus extending to a vertebral artery but thrombosis localized to a vertebral artery is rare. Occasionally thrombosis may be confined to the paramedian branches of a vertebral artery. The clinical signs with this lesion will be a hemiplegia on the opposite side with loss of postural sensibility in the hemiplegic limbs and paralysis and wasting of the tongue on the side of the lesion.

Posterior Inferior Cerebellar Artery

Each vertebral artery gives off one of these vessels. The artery curves backward around the medulla giving branches which supply a wedge-shaped area in the lateral part of the medulla, the restiform body and the choroid plexus of the fourth ventricle. Its two terminal branches

supply the inferior vermis and the posterior part of the inferior surface of the respective cerebellar hemisphere.

Occlusion of a posterior inferior cerebellar artery causes a very anatomically exact and characteristic clinical picture (Fig. 14). The onset is sudden with intense vertigo and prostration. The vertigo is due to involvement of the vestibular body due to the lesion affecting the restiform body and the cerebellar hemisphere. On the opposite side of the body there is loss of sensation to pain and temperature due to involvement of the lateral spinothalamic tract which crosses in the spinal cord. The following case illustrates the syndrome very well.

Case VII. A long-standing epileptic,

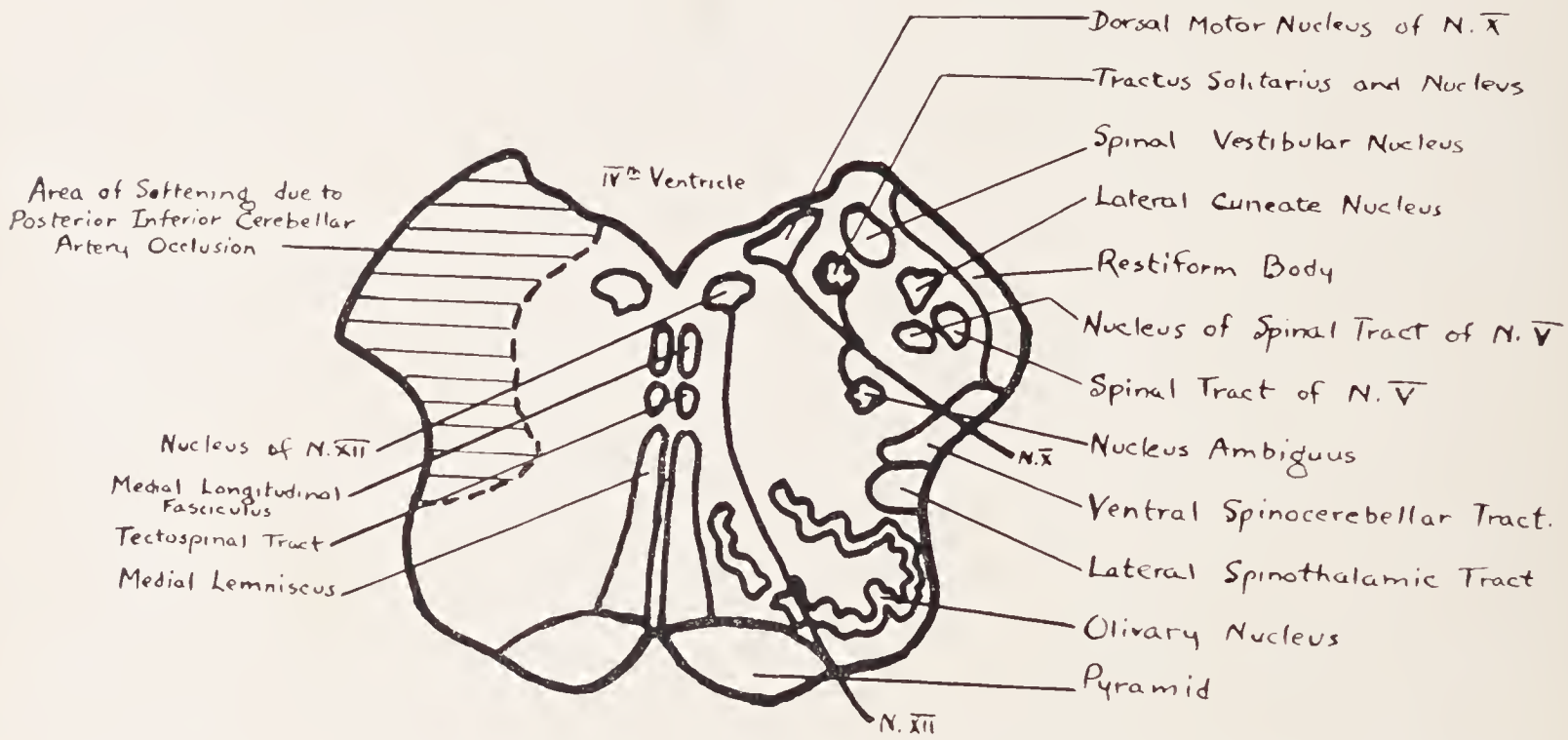


FIG. 14. Composite diagram of the medulla to show the structures involved in posterior inferior cerebellar artery occlusion.

nuclei and it is accompanied by marked nystagmus. The patient is found to be suffering from dysphagia and there is weakness of the homolateral side of the palate and pharynx due to destruction of the nucleus ambiguous (9 and 10 nerves). There is loss of taste on the homolateral side of the tongue due to involvement of the nucleus solitarius. Pain and temperature sensation is impaired on the homolateral side of the face due to involvement of the descending root and spinal nucleus of the 5th nerve. Horner's syndrome is present due to destruction of the descending sympathetic fibres. There are signs of cerebellar dysfunction on the same side of the age 50, suddenly developed severe vertigo while working. He fell to the ground without loss of consciousness. The vertigo, which was accompanied by vomiting, subsided after an hour or so. Examination showed him to be drowsy and complaining of severe left temporal headache. Nystagmus was present and the left pupil was very constricted. There was difficulty in swallowing and the palate showed a left-sided weakness on movement. The left vocal cord was paralysed. There was marked ataxia of the left arm and leg. Pain and temperature sensation was lost over the left side of the face and the right side of the body. One week after admission to hospital the patient

developed a right hemiplegia which indicated extension of the thrombosis from the posterior inferior cerebellar artery into the left vertebral artery since the paramedian branches of each vertebral artery supply the crossed pyramidal tract as well as the fillet and the 12th nucleus on the respective side. The patient's condition progressively deteriorated and he died 4 weeks after the onset.

At autopsy there was a thrombus in the left posterior inferior cerebellar artery which microscopic examination revealed to be oldest in its distal portion. More recent thrombus was seen in the proximal part of the artery and very recent thrombus occluded the left vertebral artery. There was softening in the posterior and inferior portion of the left cerebellar hemisphere and in the dorsolateral region of the medulla on the side of the lesion (Fig. 15).

Incomplete lesions due to partial occlusion of this vessel are common and the branch to the medulla often escapes so that softening is limited to the cerebellar distribution (Fig. 16). In this event the only clinical manifestations are signs of cerebellar deficit, mainly in the lower limb on the same side as the lesion.

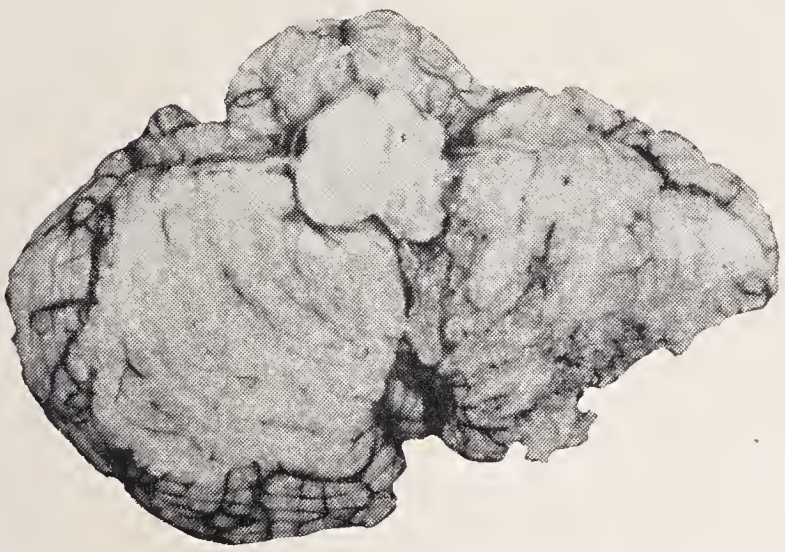


FIG. 15. Case VII. Transverse section showing the softening in medulla and cerebellum resulting from thrombosis of the left posterior inferior cerebellar artery.

FIG. 16. Softening in cerebellum in distribution of the left posterior inferior cerebellar artery. The medulla is not involved.

SUMMARY

The syndromes resulting from occlusion of the principal cerebral arteries have been discussed. In each instance an attempt has been made to correlate the clinical manifestations with the anatomical distribution of the lesion.

Cases illustrating the more common syndromes resulting from arterial infarction have been cited.

The authors wish to express their thanks to Professor C. G. Smith for his kindly advice and criticism during the preparation of this paper.

REFERENCES

1. Fisher, M.: Arch. Neurol. and Psych. 1951, 65:346.
2. Andrell, P. O.: Acta Med. Scandina. 1943, 114: 336.
3. Fisher, M.: C.M.A.J. 1951, 65: 1.
4. Cooper, I. S.: Psychiatric Quarterly 27: 317, 1953.
5. Critchley, M.: Brain 1930, 53: 120.
6. Hyland, H. H.: Arch. Neurol. and Psych. 1933, 30: 342.
7. Abbie, A. A.: The Med. Journ. of Australia 1937, 2: 564.
8. Walker, A. Earl: The Primate Thalamus, 1938. The Univ. of Chicago Press, Chicago, Ill.
9. L'hermitte, J.: J. Med. Argent. 1932, 11: 1361.

THE DAFFYDIL STORY

J. A. MACDONALD, M.D.

AUTHOR'S NOTE: This is not a scientific article. Students hopeful of memorizing precious medical pearls gleaned from this article will be disappointed —there are none—and are therefore discouraged from reading this further. I repeat . . . oh well!

THE STORY

No controversy in Medicine exists which is as fiercely fought as that concerning the origin of *Daffydil*. An allegedly reliable authority once placed the date of *Daffydil's* conception as far back as Jan. 9, 1895. This point was disputed by the Editor of *Epistaxis* of 1935 who maintained that there was positive evidence to show that *Daffydil* existed in the year 1602. He quotes William Shakespeare to prove his point:

"Daffydil that comes before the swallow dares,
And takes the winds of March* with beauty."

Dr. Bill Monk, Chairman of *Daffydil* in 1950 supposedly verified the existence of Daffydil in 1804. He cites, to illustrate his point, Wordsworth's immortal lines, written while wandering lonely as a cloud o'er vales and hills, as follows:

". . . all at once I saw a crowd,
A host of golden 'Daffydils';
I gazed and gazed—but little thought
What wealth the SHOW** to me had brought."

*In Shakespeare's time, *Daffydil* was held in March.

**Undoubtedly a clear-cut reference to *Daffydil*.

The following pronouncement may seriously stun some of the more rabid and enthusiastic Daffydilians. The bitter truth of the matter is that *Daffydil* was born in 1912. On Feb. 23 of that year an announcement appeared in the *Varsity* (yes it existed before *Daffydil*) heralding "the first annual Medical Daffydil Night in Convocation Hall on March 4, 1912." The *Varsity* proclaimed the event "a huge success" and described the evenings proceedings as "a delightful program bristling with new stunts and ideas. On entering Convocation Hall, where the entertainment was held, the names of the guests were announced as a spotlight followed them to their seats, and cards, rapidly printed, announced their arrival from the stage, as well as the eccentricities of the professors." Such was the beginning of Daffydil.

As to the origin of the word "Daffydil" there has been much conjecture. It seems that a daffydil* in the days before the talkies was related to that which can only be described for want of a better term as a "shaggy-dog" story. *Daffydil*, therefore, was purported to be a dramatization of "shaggy-dog" stories but it seems that as the years passed any anecdote at all sufficed. To increase its scope in this respect the Daffydil Committee conceived the idea of *Epistaxis* (nose-bleed), a "syncopation of Medical fun" as the Varsity described it. This illustrious publication appeared for the first time in 1916 under the editorship

*No connection with the word *daffodil*, a yellow flower.

of H. A. Hissian and E. C. Riseborough, and it was distributed at the evening's performance. *Epistaxis* contained for the reader's illumination, cartoons, anecdotes, limericks and 'poetry'.

Hidden in fine print somewhere in *Epistaxis* one could find, if so inclined, the Daffydil Programme with dramatis personnal etc.; but it required a powerful pair of bifocals to elucidate this somewhat irrelevant and unentertaining part of the publication.

In the next few years, following its inception, *Daffydil* earned an unprecedented popularity as the headlines in the Varsity attest. "Meds Daffydil Night Scores Big Success," "Daffydil Night Exceeds all Previous Attempts" and "Daffydil Rolls away Amid Whirl of Classic Drama and Stirring Modern Romance," were but a few of the superlatives showered on *Daffydil* by the *Varsity*. To what did *Daffydil* owe its uncommon success?

The secret of this success is partly attributed to the intense rivalry that existed between the four medical years, a rivalry stimulated by the promise of a Trophy to be awarded by judges, chosen from among the members of the faculty, to the year that produced the most hilarious skit. The efforts of the respective years, you may appreciate, were thereby intensified and the result was bedlam.

Contributing no less to the general success and appeal of *Daffydil* was the completely uninhibited nature of the production which saw no parallel (we are led to believe) in those quiescent days. We have only the printed word of the *Varsity* and the unbiased statements of innumerable Graduates to rely upon, but the descriptions of the skits support this opinion. "Operation scenes" reports the *Varsity* "in which were portrayed all the callousness, indifference and dogmatism of the profession" were quite popular at the time. In one operating scene, an amputation of a leg, the late Dr. Frank O'Leary acted as patient. The intense realism created during the procedure caused many of the young ladies of the audience to swoon in their escorts' arms, which was the result desired. Little did the female audience realize that Dr. O'Leary had an artificial leg and that he was not averse to permitting the surgeon to saw completely through the wooden limb while he let out agonizing screams of pain. This skit was deemed "successful" by the Committee. It seems that in these operating scenes, any device was justified if it achieved realism or if it approached the grotesque. In 1914 the *Varsity* portrayed another operation described as "successful". "When the incision was made a blood-red membrane protuded which expanded until it reached the dimensions of an ordinary balloon, when it suddenly exploded with an appalling sound," much to the delight of the medical students in the audience. Parodies and impersonations of professors were likewise of tremendous appeal but it is not known to what extent their antics differed from recent imitations of Professors. Less popular, but occasionally included in the program, were violin solos, recitations and the like which received scant praise from the *Varsity* reporters.

In 1917 *Daffydil* was cancelled after five consecutive performances because of a coal shortage which necessitated closing of all University buildings. The following year however it returned with its partner in crime—*Epistaxis*.*

From *Epistaxis*, a reliable source,

*Past editions may be obtained from the author upon request.

much information has been obtained revealing the Thespian talents of various personalities. This information will now be passed on to posterity. In 1933 the class of 3T7 in its presentation of a skit entitled "Spreading it Even" revealed a versatile student by the name of W. Mustard, who played the several parts of (1) a student, (2) Marya the wife, (3) Dracula and (4) a street cleaner in successive scenes. The same student it appears, also characterized Charlie McCarthy with the able assistance of a classmate who portrayed Edgar Bergen. (Who said that Milton Berle was versatile?) Another student in the same production, one J. D. Hamilton it is revealed, portrayed a T.G.H. nurse whose rolling eyes caught the fancy of many of the medical students.

It is also interesting to note references in *Epistaxis* to Dr. Alan Brown of which there was one of note in *1924* quoting him on the advantages of breast milk over cow's milk. One is led to believe that this medical fact (and the joke that accompanies it) *has* been firmly implanted in the minds of generations of students.

Epistaxis was particularly astute in several of its predictions. In 1929 this journal predicted that "for the next few years, Professor Bailley will mumble incoherently to approximately 150 bewildered students about the promiscuous and very prolific Sodrophila Gelanomaster. He will pretend to read from the same set of blank cards which he has used since time immemorial." Again in 1946 this indomitable publication predicted that "Professor 'Itchy' Ham will thrice weekly present his imitations of a flea-infested fakir telling a bed-time story, and will conveniently darken the room at the end of his lecture for the benefit of the class wolves," and that "Prof. Dick Tracy Rogers will continue to give first year students the latest news on low-life in Ontario." *Epistaxis* also vigorously protested the callous suppression by the powers that be in the Path. Chem. department of one of the greatest advances in Medical science, to wit, the discovery of a new type of filter paper which had the properties of "automatically giving tests for sugar, acetone, blood, bile, cerobilin, and urobilin" which thereby would have eliminated two years from the medical course and six months of interneship. Apparently this was deemed not to be in the better interests of the student.

In 1940 however, by decision of the Caput, *Daffydil* and *Epistaxis* were banned from the Campus. Permission was withheld to produce the show and to publish *Epistaxis* in the face of campus-wide criticism which labelled *Daffydil* and *Epistaxis* as "debasing institutions." The script of that year had been submitted to the Caput and returned as "undesirable." The resignation of the Daffydil Committee followed shortly thereafter.

Epistaxis was never again to return to the campus but *Daffydil* reappeared in 1946 with a flourish. I say with a flourish, but it seems that *Daffydil* made considerable noise that year yet it failed to capture—for better or for worse—the spirit that had characterized previous performances. Many a Daffydilian reluctantly but sincerely admitted this fact.

It was not until 1947 that the author had the privilege of attending *Daffydil* for the first time. One was not impressed by music nor was one left breathless by the chorus line. However, in my humble estimation the production was a laugh-a-minute affair. The memorable event

of that year's production was the portrayal of Frankenstein by J. R. Evans of 5T2. This was executed so realistically, I recall fondly, that each performance waked piercing screams from the frightened women in the audience. Boris Karloff could not have done as well.

Also in that year *Daffydil* was featured in New Liberty Magazine. It seems that this publication concentrated less on *Daffydil* as a production and more on several of the chorus girls who were effectively photographed (to advantage) from many different angles.

In the year 1949 *Daffydil* achieved a slightly professional touch with the production of a movie, color and sound included. The movie was produced by Manny Rotenberg of 5T2 and it was truly ingenious and highly entertaining. The movie illustrated various aspects of Toronto with its "friendly people, wide-open parks, sunny playgrounds and beautiful tree-lined boulevards" as well as the highlights of the medical curriculum.

A musical trend has been evident since the performances of 1950 and 1951 which concentrated less upon repartee and more upon original musical production numbers. This trend reached a peak in this year's presentation of an operetta entitled "The Anomaly" with music, lyrics and dialogue as refreshing as a breath of springtime air. Messrs. S. T. Bain, S. Greben and S. Freeman of 5T3 deserve the bouquets for this delightful musical. Dean MacFarlane, in a letter to the Medical Society expressed his congratulations to the Daffydil Committee as follows. "The second half (the operetta) was particularly entertaining and showed much evidence of originality and talent. I have thought for many years that in the Faculty of Medicine there is sufficient versatility and ability that such a show could be produced and this year we have proof of that conviction." Truly, the traditions of *Daffydil* have been upheld.

Acknowledgement

I should like to express my thanks to C. Roland whose diligence in ferreting out material couched in the dusty files of the *Varsity* made the preparation of this article possible.

BIBLIOGRAPHY

The Varsity
Epistaxis

THE MUSCLE RELAXANTS

H. I. AXELROD, B.A., M.D.

Good muscular relaxation is one of the essentials in the anaesthetic management of the patient undergoing surgery. The earliest clinical use of curare, the first of the muscle relaxants, dates from 1866 when it was used to control the convulsions of epilepsy. In 1935 the active principle d-tubocurarine chloride was isolated by King (1) from the plant chondodendron tomentosum. In 1939 Bennett (2) introduced d-tubocurarine chloride to clinical medicine. It was left to Griffith (3) in 1942 to introduce curare into anaesthesia. This opened a new era in curare therapy.

Nerve-Muscle Physiology (4)

The normal resting neuromuscular unit consists of nerve fibrils, a polarized motor end plate and muscle fibres (fig. 1).

Transmission of nerve impulse causes liberation of acetylcholine (Ac) at the ends of the nerve fibrils. The acetylcholine depolarizes the end plate, thus initiating muscular contraction (fig. 2).

In the restitution of the neuromuscular unit, acetylcholine esterase (Es) destroys acetylcholine and the motor end plate is repolarized. The unit is now ready for the transmission of the next impulse (fig. 3).

Blocking of the myoneural junction can be achieved in three main ways:—

1. The nerve fibrils may be rendered unable to release acetylcholine.
2. By inhibiting the physiological depolarization of the end plate caused by acetylchline. This includes the Curare (C) like groups (fig. 4).
3. By producing persistent depolarization and thereby preventing the physiological depolarization-repolarization sequence caused by the acetylcholine-choline esterase system. This includes the Syncurine (S) like compounds (fig. 5).

THE IDEAL MUSCLE RELAXANT (5)(6)

The ideal muscle relaxant should be capable of:—

1. Specificity of action.
2. Action of sufficient duration to permit prolonged muscular relaxation during major surgery.
3. Not interfering with normal metabolic processes, normal patterns of respiratory or cardiovascular action.
4. Prompt resumption of muscular reactivity at the termination of operation.
5. Being rapidly metabolized in the body to innocuous degradation products.
6. Showing no toxic side effects or complications.
7. Brief action for use in endotracheal intubation, electric shock therapy and the reduction of fractures.
8. Wide margin between muscular relaxation and respiratory arrest.

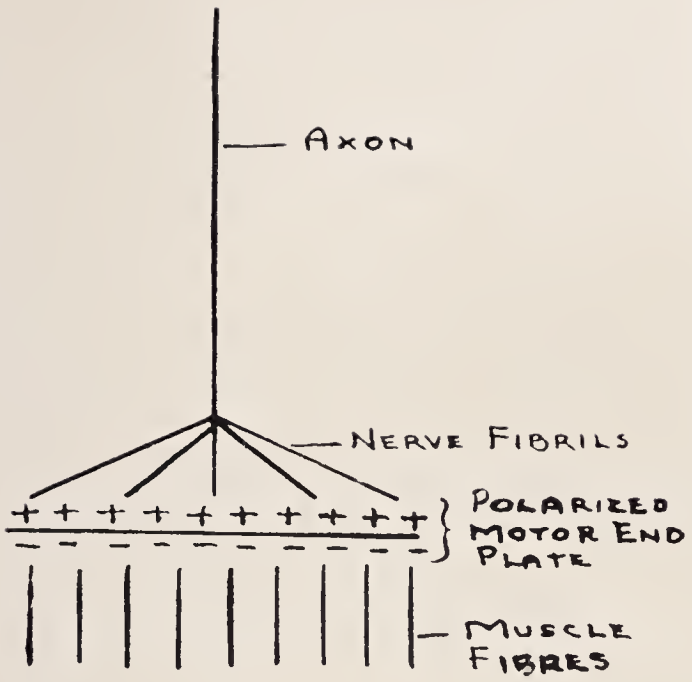


FIG. 1

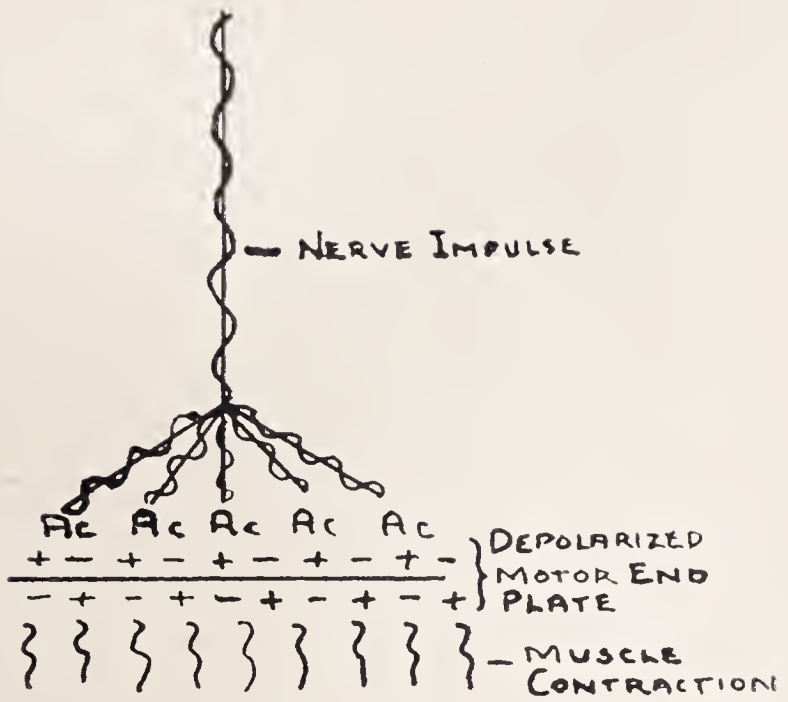


FIG. 2

PHARMACOLOGY (5)

It is thus seen that pharmacologically and clinically the neuromuscular blocking agents can be divided into two main groups, the curare-like group and the syncurine-like group. Numerous compounds have been recently synthesized that are also capable of blocking neuromuscular transmission. These are characterized by the presence of more than one quaternary ammonium group placed about 15 A apart in the molecule. Gallamine Triethiodide (Flaxedil) and the dimethyl ether of d-tubocurarine chloride (Metubine) belong to the curare-like group. Decamethonium bromide (syncurine) and succinylcholine, composed of two molecules of acetylcholine and sold as the chloride or bromide (Anectine (CL), Scoline (CL), Brevedil (Br_2))

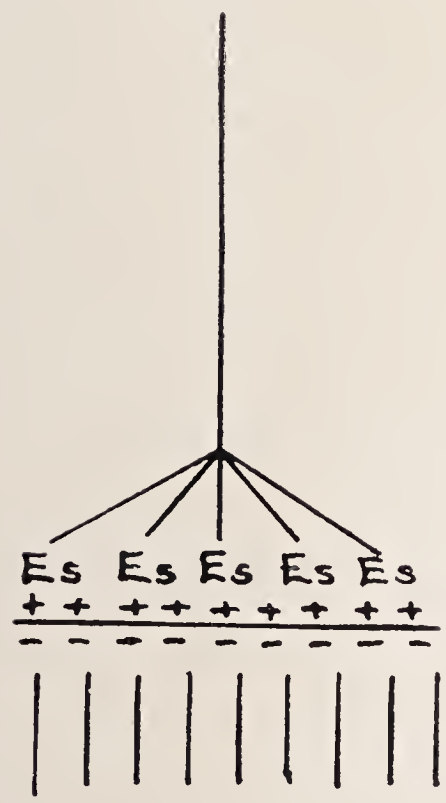


FIG. 3

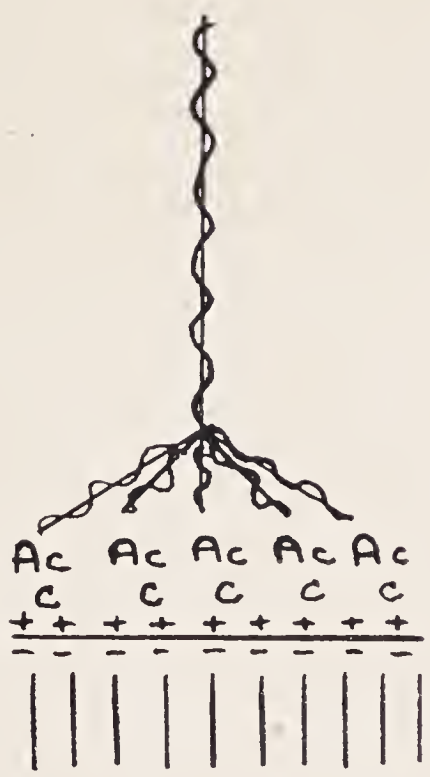


FIG. 4

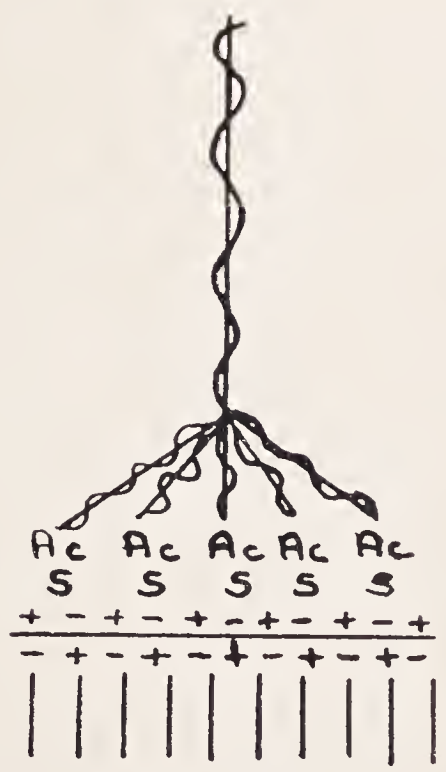


FIG. 5

belong to the syncurine group. Benzoquinonium chloride (Mytolon) is an intermediary compound in its action. All these compounds, adjuncts to good anaesthesia, are freely soluble in water, readily miscible with other drugs, can be sterilized by autoclaving, and can be stored at room temperatures with very slight loss of potency for prolonged periods.

On intravenous administration only the striated skeletal muscles are affected and in the following sequence:—muscles of the face, pharynx, larynx, peripheral limb muscles, abdominal, intercostal and finally the diaphragm. On recovery, the reverse takes place. The initial dose of muscle relaxant is determined on an empirical basis and the vigor, age and muscular development of the patient. Considerable variation in the sensitivity of different persons to muscle relaxants exist. Controllability, which in turn depends on the fate of the drugs in the organism, is the most important factor in determining the indications and contraindications of the drug.

A. THE CURARE-LIKE GROUPS (14)

This includes d-tubocurarine chloride, the dimethyl ether of d-tubocurarine (Metubine) and gallamine triethiodide (Flaxedil). Since curare is the parent compound, it will be discussed in some detail. The doses mentioned are those for the average adult.

Curare

Curare or d-tubocurarine chloride pentahydrate, a crystalline salt of definite composition (C38 H44 06 N2 CL2 5H20) is a purified chondodendron tomentosum extract which can be standardized by physical and chemical methods and prescribed in terms of weight (mgms.) of the pure drug. It is biologically assayed by the rabbit head drop test. Essentially this is a test for failure of neuromuscular transmission. A series of injections of curare is given fifteen seconds apart. The end point of the assay is the inability of the rabbit to raise its head in response to a physiologic stimulus. By comparison with the activity of a standardized preparation of crystalline d-tubocurarine the potency of any curare sample may be measured. The common method of administration is intravenously. The initial dose varies between 9-12 mgm. The maximum effect is noted in 1-4 minutes with duration lasting from 10-25 minutes. A single intravenous dose can be repeated, but in smaller amounts as a cumulative effect has been noted. Similarly if ether is to be used, smaller doses of curare should be given as ether in itself has a curare-like action. The drug is excreted, largely unchanged, by the kidneys.

The side effects include blocking at the autonomic synaptic transmission and the release of histamine (7) (8) (9). This histamine release is in part, responsible for the bronchospasm and hypotension that are frequently noted with curare. It has been suggested that in patients with allergic conditions such as asthma, hay fever and known drug allergies as well as in patients in whom paralysis of autonomic ganglia is to be avoided, curare and its derivatives should not be used. The hypotensive effect results in part from histamine release, in part from blocking action at sympathetic ganglia or through the muscular relaxation with its consequent diminished venous return. It may be possible that the histamine-like release can be avoided by the pre-operative administration of antihistaminics.

Flaxedil (Gallamine triethiodide) (4)

The initial intravenous dose is 40-80 mgm., with a maximum effect in 3-5 minutes and duration of 25-25 minutes. Repeated doses do not show a cumulative effect and it can be used freely in the presence of ether. It too is excreted largely unchanged by the kidneys. It does not cause a histamine release with its consequent bronchospasm and hypotension, and there is little or no action on the autonomic nervous system. It has however, an atropine-like effect on the cardiac vagus, so that a tachycardia is often present. 80-100 mgm. Flaxedil are equivalent to 15 mgm. curare.

Antidotes:

Since these drugs affect intercostal as well as diaphragmatic muscles, apnoea is often observed. Methods for artificial respiration should always be at hand in the presence of these drugs. Prostigmine, eserine, D.F.P. (di-isopropyl fluorophosphate). Tensilon (edrophonium chloride) act by inhibiting acetylcholine esterase, thus allowing for the accumulation of acetylcholine. Recently (11) a group of cholinergic compounds which are quaternary amines have been investigated as anticurarizing agents. Their action is postulated on a displacement of curare at the motor end plate.

B. THE SYNCURINE-LIKE GROUP (12)

Syncurine

This consisted of two quaternary ammonium molecules separated by an aliphatic straight chain of ten carbon atoms. Hence the name decamethonium bromide. The end result following the administration of syncurine is the same as that produced by curare, but the mechanisms of action of the two agents, as stated previously are directly opposed. Syncurine prolongs depolarization whereas curare prevents it. Its action resembles that of acetylcholine which if allowed to pile up at the myoneural junction, blocks the muscle response. Since syncurine acts in this manner it should theoretically be counteracted by d-tubocurarine. In the laboratory such is the case.

The initial intravenous dose is 1-4 mgm. with a maximum effect noted in 4-6 minutes and a duration of 20 minutes. There is no cumulative effect and the drug may be used cautiously with ether. In therapeutic doses it shows no effect on autonomic synaptic transmission, nor is there an histamine effect. It, like the others is excreted largely unchanged by the kidneys. Four mgm. of syncurine is equivalent clinically to 20 mgm. curare.

The intravenous injection of syncurine as with succinylcholine is followed by fasciculatory muscle movements. These, caused by the depolarizing action of the drug, can be avoided by a slow rate of injection.

Succinylcholine (4)(5)(6)

It consists of two molecules of acetylcholine and is used as the bromide, iodide or chloride.

It is an ultra short acting muscle relaxant. The initial intravenous dose is 15-45 mgm. with a maximum effect noted in 1-2 minutes and a duration of 3-5 minutes. There is no effect on autonomic synaptic transmission nor is histamine liberated. It does not show cumulative action, nor is it potentiated by ether. It has a slightly vagolytic effect and its intravenous administration is followed by fasciculatory muscle movements. It can be given as intermittent single intravenous injections but more

commonly as a continuous 0.16 to 0.20% intravenous drip. The drug is rapidly hydrolysed by both the plasma cholinesterases and the true acetylcholine esterases to pharmacologically insert choline and succinic acid. It is also rapidly hydrolysed by alkaline solutions and therefore loses potency rapidly if mixed with thiopental sodium. Succinylcholine acts independently of the presence of either syncurine or curare, but if given while either of these drugs is exerting its muscle relaxing effort, it would produce an added degree of muscular relaxation. It should not be given to those having a decreased cholinesterase activity as occasionally seen in patients with liver disease, malnutrition, anaemia or poisoning with some polyphosphate insecticides (13).

Antidotes:

As with all muscle relaxants, the prime requisite is artificial respiration. The use of prostigmine DFP and Tensilon are contraindicated, but if used, they tend to prolong the action of syncurine and succinylcholine.

Indications for use of Muscle Relaxants

1. Surgical procedures
2. Electroshock therapy
3. Control of tetanus

Contra-Indications

These are relative and not absolute, and depend on the experience and knowledge of these drugs by a competent administrator.

1. Absence of, and the inability of the administrator to perform efficient artificial respirations.
2. Pulmonary disease: asthma, emphysema.
3. Myaesthenia gravis.
4. Nervous system Diseases: poliomyelitis, neuritis, amyotrophic lateral sclerosis, etc.

ACKNOWLEDGEMENTS

I am indebted to Professor S. Campbell, Department of Anaesthesia, University of Toronto, and to Dr. R. Chaplin, Toronto East General & Orthopaedic Hospital, for helpful criticism in preparation of this paper.

REFERENCES

Collins, Vincent J.: Anaesthesiology, Lea and Felsiger, Philadelphia, 1952.

Best, C. H., and Taylor, N. B.: The Physiological Basis of Medical Practice. 5th edition. The Williams and Wilkins Company. Baltimore.

Goodman, Louis and Gilman, Alfred: The Pharmacological Basis of Therapeutics. The Macmillan Company of Canada, 1952.

(1) King, H.: J. Chem. Soc. 2:1381, 1935.

(2) Bennett, A. E.: Preventing Traumatic Complications in Convulsive Shock Therapy by Curare. J.A.M.A. 114:332 (January 27th), 1940.

(3) Griffith, H. R., and Johnson, G. E.: The Use of Curare in General Anaesthesia. Anaesthesiology, 3:418 (July), 1942.

(4) Foldes, F. F. et al.: Synthetic Muscle Relaxants in Anaesthesia. J.A.M.A. 150: 1559, December 20th, 1952.

(5) Foldes, F. F. et al.: Succinylcholine: A New Approach to Muscular Relaxation in Anaesthesia. Proceedings of the Canadian Anaeshetists Society, 1952.

(6) Little, David, M. et al.: Succinylcholine. A Controllable Muscle Relaxant. Anaesthesia and Analg. 32:171 (May-June), 1953.

(7) Alan, M. et al.: Liberation of Histamine from Skeletal Muscle by Curare. J. of Physiol. 95:148 (February 14), 1939.

(8) Grab, D. et al.: On Certain Vascular Effects of Curare in Man. Bull., Johns Hopkins Hospital, 80:299 (June), 1947.
(9) Landmesser, C. M.: A study of the Bronchoconstrictor and Hypotensive Actions of Curarizing Drugs. Anaesthesiology, 8:560 (September), 1947.
(10) Walton, F. A.: Flaxedil, A New Curarizing Agent. C.M.A.J. 63:123 (August), 1950.
(11) Artusio, J. F. et al.: Studies on Inter-Relationships of Certain Cholinergic Compounds. J. Pharm. and Exper. Therap. 227:100, 1950.
(12) Paton, W. D. M.: Pharmacology of Decamethonium. Ann. New York Acad. Soc. 54:347 (October 30), 1951.
(13) Correspondence, Lancet, Vol. II, No. 3, July 18th, 1953.
(14) Unna, E. W. et al.: Evaluation of Curarizing Drugs in Man. Jour. Pharm. and Exper. Therapy, 98:318, 1950.

If many drugs are used for a disease, all are insufficient.—Osler.

THE UNIVERSITY OF TORONTO
MEDICAL JOURNAL
(AN UNDERGRADUATE PUBLICATION)

FACULTY ADVISORS
E. A. Linell, M.D., MANC.
E. B. Tovee, M.D., M.S., F.R.C.S.(C.), F.R.C.S. EDIN.
W. R. Feasby, B.A., M.D.

EDITOR-IN-CHIEF
Miss J. H. Griffin, B.A.

ASSOCIATE EDITOR
C. A. Smythe

MANAGING EDITOR
R. E. White, M.A.

ASSISTANT EDITORS
J. C. Stears — J. W. Goodwin
I. B. Rosen — J. Wagner
W. J. Kokeny

EDITORIAL ASSISTANTS
A. Goldberg — W. C. Proctor
K. O. McCuaig — Miss S. Saunders

FEATURES
Editor: W. H. McCrae

ABSTRACTS
Editor: F. P. Ceresney
J. D. T. Ainslie

ADVERTISING
Manager: C. G. Roland
Assistant: J. F. Morgan

CIRCULATION
Manager: P. C. F. Moore
Assistant: J. C. Alexander

This journal is published six times during each year, between October and March, by the Medical Society of the University of Toronto, to serve as a medium for student expression and to bring to each student recent articles of scientific interest.

$2.50 per volume **50c per copy**

Authorized as Second-Class Mail
Post Office Department, Ottawa

EDITORIAL

COMPULSORY INTERNESHIP

The recent resolution of the General Medical Council of Canada stating that after January 1, 1954 no graduate in medicine will receive a license to practise until one year of interneship has been satisfactorily completed has caused considerable discussion among the students of this university.

One of the questions being asked is how this will effect the interne and his practice of medicine within the hospital scene—will he be allowed to write prescriptions, sign certificates, etc., without first consulting some senior person. Much speculation has been aroused as to whether the ruling will seriously effect those planning to interne in the United States. Will it jeopardize the possibility of obtaining such interneships and will they be recognized by the licensing authority upon their termination? However, the greatest fear seems to be that such a ruling may, in time, allow the licensing board to limit our freedom to choose the place in which we interne.

It would seem to this observer that there is much ado about nothing in this regard. If we sit back and look at the question impartially we will see that we of this University are more fortunate than those in many centers—we still write our Council Examinations before, and not after, interning. The total effect of this ruling seems to be merely to make one year of interning obligatory, and both we and our future patients will benefit. Any of us who go into General Practice and later decide to specialize will have completed the required year, and our patients, when we do get into practice, will receive more skilled care than we could have given them had we not interned. G.

BIRTH INJURIES

JOHN PALMER, M.D.*

BIRTH trauma to almost every structure of the body has been reported at one time or another. The more common injuries will be discussed under the following headings.

I. *Obstetrical Paralysis*
   (1) Brachial plexus
   (2) Facial nerve
   (3) Spinal cord

II. *Fractures*
   (1) Fracture or slipped epiphysis due to excessive trauma
   (2) Fracture secondary to increased fragility of bone
   (3) Congenital fracture of tibia leading to congenital pseudo-arthrosis

III. *Head Injuries*
   (1) Hemorrhage
   (2) Fracture skull
   (3) Cephalohematoma

IV. *Soft Tissue Injuries*
   (1) Visceral
   (2) Rupture of the bowel
   (3) Torticollis

I. *Obstetrical Paralysis*

1. BRACHIAL PLEXUS

Paralysis involving the arm is usually one of three varieties.

(1) Erb's or upper arm type.
(2) Klumpke's or lower arm.
(3) Whole arm type.

In Erb's series of 473 cases, 400 were of the upper arm type; 64 whole arm, and 9 mixed.

ERB'S PALSY results from downward traction on the arm or from undue traction on the head when the delivery of the shoulders is difficult. The 5th and 6th cervical roots are involved to a varying degree of severity. Mild injury results in edema and a transient block with temporary loss of conduction; more severe injury may produce a lesion in continuity with delayed and indefinite recovery, or there may be complete division.

The Clinical Features. The hand hangs loosely at the side. The forearm is pronated; the elbow slightly flexed; the upper arm internally rotated; and the child is unable to abduct the arm. A paralysis of the deltoid, supraspinatus, biceps, coracobrachialis, and brachioradialis is present.

Contractures soon develop from the unopposed action of the adductors and internal rotators of the shoulders. Occasionally paralysis of the diaphragm occurs when the phrenic nerve (C4) is involved. This can be diagnosed by fluoroscopy.

KLUMPKE'S OR LOWER ARM TYPE

Roots C8 and T1 of the brachial plexus are involved. It is said to result from undue traction on the arm above the head. There is often paralysis of the whole arm followed by quick recovery of the muscles of the upper arm, but

*From a paper presented at the Hospital for Sick Children, Toronto.

residual paralysis involving the muscles of the hand and fingers. A Horner's syndrome is usually present.

WHOLE ARM TYPE occurs only from extreme trauma, usually with avulsion of the spinal roots from the cord.

Prognosis

The extent of recovery is impossible to predict at an early date. It of course depends on the severity of the injury. If recovery has not begun by six months, recovery will not occur. As a rule the Erb's type does well and recovery is progressing well or complete by six months. However the Klumpke and whole arm types usually do poorly.

Management

Xrays should be taken to rule out the occasional associated injuries—fractured clavicle or humerus or slipped epiphysis.

Treatment is begun early and is directed to prevent contractures and to prevent additional traction on damaged nerve trunks.

The arm is immobilized in an abduction splint with the arm abducted, externally rotated, the elbow flexed to a right angle, and the forearm supinated. The splint is retained for approximately six months, unless the palsy has recovered. During this time the splint is removed two or three times daily so that the mother may passively exercise the limb and encourage the infant to move it. Physiotherapy is useful. A close watch should be kept for contractures, preventing them by full range movements or stretching if necessary. After this the splint may be used at night and the child encouraged in voluntary movement during the day.

The problem of exploratory operation arises if there is no sign of recovery in four to six months' time.

The operation is technically difficult. The lesion is usually found at the junction of the 5th and 6th roots, which are generally enveloped in scar tissue. This is fully excised. Occasionally the tear is in the intervertebral canal or at the junction of the roots with the cord.

According to Speed and Smith exploration is seldom justified. Muscle power has either returned sufficiently to warrant continuation of conservative measures, or paralysis is so extreme that little can be gained by exploration.

Otherwise the surgical treatment consists of correction of deformities.

A subscapularis release is used frequently for correction of severe internal rotation contractures. Dr. Mustard believes it is advisable to do this procedure fairly early, around the age of 2–3, before secondary deformities of the head of the humerus occur.

Some authorities advocate osteotomy of the humerus with lateral rotation of the lower fragment, or a combination of both methods. An osteotomy is usually necessary and more satisfactory in older children.

2. PARALYSIS OF THE FACIAL NERVE

This occurs more frequently than does Erb's palsy. It is usually due to pressure from forceps blades on the nerve. The paralysis almost always recovers spontaneously within two to three weeks. The few that do not recover are either of central origin or due to complete division. These can be improved by plastic procedures at a later date.

3. SPINAL CORD INJURIES

Spinal cord injuries are uncommon, and are usually the result of excessive traction in breech deliveries. Fracture of the spine, usually the 6th cervical, or haemorrhage may compress the cord.

The paralysis is of variable severity and the distribution depends on the nature of the injury.

II. *Fractures*

1. Due to Excessive Trauma

SLIPPED EPIPHYSIS

Displacement of the upper humeral epiphysis can produce a picture similar to Erb's palsy.

The epiphysis rotates backward and inward and the arm assumes the position of protective immobilization against the chest. This results in a contracture similar to an Erb's, with limitation of external rotation. Treatment is the same as in an Erb's palsy—abduction splint, followed if necessary by subscapularis release or osteotomy.

Slipped lower humeral epiphysis is rare. It is diagnosed by the presence of pain, limitation of movement and swelling of the elbow. The centre of ossification has usually developed in the head at birth but it does not develop in the distal end until the end of the first year. Radiological diagnosis is possible, however, about two weeks after the injury, due to ossification of the subperiosteal hematoma.

Treatment: Gentle axial traction is applied and the limb flexed and placed in a sling. Results are always good.

Displaced lower femoral epiphysis is uncommon. It can be diagnosed radiologically. The epiphysis is displaced posteriorly. Overhead traction as in fracture of the femur is most satisfactory. Even without treatment the femur is radiologically normal in two to three years.

FRACTURE OF SHAFT OF HUMERUS

This is fairly common, usually following breech deliveries due to attempts to deliver the extended arm. The fracture site is usually middle third and is not infrequently accompanied by radial palsy.

Treatment is simple. The arm is strapped to the chest over padding, thick enough to maintain some abduction. Union is usually solid in three to four weeks. Outward angulation may occur but this straightens eventually.

FRACTURE OF FEMUR

This usually occurs in delivering the extended legs in a breech or in extracting the child in Caesarian section. Obvious angulation is present. The proximal fragment is usually markedly flexed.

Treatment is simple. The method of overhead suspension of both lower limbs is used. Fractures unite without angulation, and the nursing care of the infant presents no problem. The fracture unites in four to five weeks.

FRACTURE OF CLAVICLE

Fracture of the clavicle is common, usually of the middle third. The infant refuses to move the arm or cries when it is moved. Treatment is not a problem. A pad in the axilla and the arm strapped to the chest, or a strip of elastiplast over the fracture site is satisfactory.

2. Secondary to Increased Fragility

Fractures due to *Osteogenesis Imperfecta* are rare. The fractures are usually multiple. There is a marked hereditary and familial tendency, and is usually associated with blue sclerotics. The bones are light and fragile; the trabeculae widely separated and the cortex thin. If the child survives delivery, treatment is the same as in other fractures and rapid healing occurs.

3. Congenital Pseudoarthrosis

Congenital pseudoarthrosis of the tibia is characterized by fracture of the tibia

apparently not associated with trauma, with increased callus formation and non-union. Green and Rudo believe that all these cases are due to neurofibroma. However this is not universally accepted. Probably the best approach to the problem is that described by A. W. Farmer. He uses cutaneous-bone pedicle grafts, which behave like living bone. Watson-Jones reports success by the use of double onlay grafts, in older children.

III. *Head Injuries*

1. Hemorrhage

INTRACRANIAL injuries are important because of their frequency and because of the after-effects in a high percentage of the survivals. Intracranial hemorrhage if massive, is usually due to rupture of one of the large venous sinuses or the vein of Galen. Multiple small hemorrhages may occur within the brain.

EXTRADURAL HEMORRHAGE, usually associated with fracture, results from rupture of the thin-walled veins of the dura, and occasionally of the middle meningeal artery. In the adult the middle meningeal artery is the common source. Gradual loss of consciousness occurs with evidence of compression, and deep shock. 200-400 ccs. of blood may accumulate, and this in a small infant causes profound shock. Treatment consists of supportive therapy, followed by burr holes.

SUBDURAL HEMORRHAGE is a relatively common condition and the source of a high morbidity if neglected. Mental deficiency is a uniform result if not properly recognized and treated. It is caused by direct trauma to the head, usually associated with cephalo-pelvic disproportion or pricipitous births. However the absence of a history of trauma should never influence the diagnosis. A deficiency in vitamin C, vitamin K, or any other disease giving rise to an increased bleeding tendency will increase the possibility of a subdural clot formation. The hematoma usually results from bleeding from cortical veins passing from the cerebrum to the dura.

Symptoms:

There is no characteristic picture. However there are common symptoms and signs which are highly suggestive.

1. Convulsions are common. These may be localized to one side, one extremity or to the face—usually are generalized and accompanied by loss of consciousness.
2. Poor weight gain, refusal of feedings, irritability.
3. Irregular temperature swings.
4. Abnormal increase in head size.
5. The neurological examination is difficult to assess in the infant. However hypertonicity is very common.
   —hyperactive reflexes, spastic extremities and ankle clonus.
   —paralysis is present occasionally.
   —changes in the fundi are usually not marked—small retinal hemorrhages being the most common finding.
6. The enlarged head cannot be differentiated from hydrocephalus secondary to obstruction of cerebrospinal fluid circulation, by clinical examination. The prognosis is vastly different and the differentiation is important.

   The other features present with the enlargement are bulging of the fontanelles and downward turning of the eyes.

The important fact to remember is that frequently the only finding is an infant appearing ill and malnourished.

Diagnosis: is based on the subdural tap. The tap is made at the lateral limits of the anterior fontanelle, or if closed, along the frontal suture line. Bilateral taps are done at the first sitting. The type of fluid obtained varies from grossly bloody to a straw-coloured fluid. Bilateral taps are always done—50% of subdurals are bilateral.

Treatment

Daily taps may be continued for 1-2 weeks depending on the degree of improvement obtained. As well as the gradual decompression, supportive therapy—blood, vitamins, proper diet, is stressed.

The second step is bilateral trephination. The size of the membrane is noted and if small occasionally can be removed through the burr holes. The subdural fluid is evacuated as completely as possible. If solid clot is present or if the membranes are large, bone flaps are done at this time or within the next week and all parts of the membrane and clot removed. It is most important in infants to remove all of the membrane because the rapid increase in brain volume during the first two years must be unrestricted to avoid cerebral atrophy.

2. Fracture of the Skull

Fracture of the base of the skull is uncommon and when present is usually associated with severe brain damage and hemorrhage. The prognosis is grave. However depressed fracture of one or more bones of the skull is fairly common. It is usually a spoon-shaped depression just posterior to the coronal suture. Most of these disappear in a few weeks. If the depression is more than a few mm. and there are signs of cerebral compression, the indentation should be elevated. This may be done through a small traphine hole at the periphery of the indentation. A curved director is then passed through the opening and the depressed bone levered back. If difficult, the whole fragment may be exposed through a semicircular skin flap.

3. Cephalohematoma

This is due to periosteal injury, usually of the parietal bone. The hematoma forms subperiosteally and has a definite palpable edge. It may not appear for some days or hours after delivery. Calcification occurs first around the edges, making it feel very much like a depressed fracture.

If the tumor is small no treatment is necessary. However if large, it is best to aspirate the blood and inject Wydase into the cavity.

IV. *Soft Tissue Injuries*

1. Visceral

Injuries to the abdominal organs occur, following difficult labours, especially in the large infant.

The liver, the adrenal and rarely the spleen may be torn resulting in intra-abdominal hemorrhage. The child may appear normal at birth, until the hematoma ruptures and further hemorrhage takes place.

Findings in reported cases are: sudden onset of pallor, breathlessness, tachycardia, abdominal distension and dullness. Paracentesis may yield dark blood.

Treatment consists of immediate transfusion and Vitamin K. Laparotomy and repair may be necessary.

2. Rupture of the Bowel

Perforation of the intestines can occur. This not explained satisfactorily by trauma. However it does occur in the neo-natal period and without evidence of obstruction. Perforation peritonitis re-

sults in vomiting, cyansis, rapid grunting respirations and abdominal distension. X-ray reveals pneumo-peritoneum and distended loops. Supportive therapy and operative closure of the perforation is necessary.

3. Torticollis

Muscular torticollis or congenital wry neck is probably due to excessive stretching or tearing of the sternomastoid muscle during delivery. Many of the infants have been breech deliveries (50%) and frequently show evidence of other trauma. Others suggest that the prenatal position may cause the deformity, and the damage to the sternomastoid is an ischemic fibrosis. It is true that on examination of the tumors no evidence of old blood is found and no hemosiderin found with iron stains. It is probable that injury to the normal muscle or to a muscle already maldeveloped and shortened as a result of intrauterine position produces a necrosis of the muscle and the fibroblastic replacement is an attempt at repair. The mass is a fibroma not a hematoma.

The first finding is a hard tumor mass in the sternomastoid which appears in the first two weeks of life. The mass enlarges and the head becomes pulled to that side. If the tumor is small and the deformity minimal, the head spontaneously straightens and may not cause trouble later unless a period of rapid growth occurs. If more severe, even though the mass does not become larger, progression of deformity occurs. These are the cases that should have early operative correction.

The mild or borderline cases here, are treated by daily stretching of the muscle, first by a physiotherapist then by the mother. This is often sufficient. If the deformity persists, these and the more severe cases are operated upon. This is preferable to waiting until deforming changes in the cervical spine, face and head occur. The procedure used here is open tenotomy of the sternomastoid followed by physiotherapy. Subcutaneous blind tenotomy is dangerous.

REFERENCES

Basic Texts:

(1) Management of the Newborn. Parmalee (Year Book Publishers)
(2) Fractures and Joint Injuries. Watson Jones (Livingstone)
(3) Acute Injuries of the Head. Rowbotham (Livingstone)
(4) Orthopaedic Surgery. Mercer (Arnold)

1. Obstetrical Shoulder Trauma. Scaglietti. Surg. Gyn. & Obs. 868. 1938.
2. Nonfatal Obstetric Diseases of the Newborn Infant. Paralysis and Fractures. Rev. Gyn. & Obs. 1:398. June, 1950.
3. Subdural Hematoma in Infancy. Ingraham & Watson. J. of Paed. Jan.. 1944.
4. Extradural Hematoma in Infancy and Childhood. Ingraham, Campbell & Cohen. J.A.M.A. 140:1010, 1949.
5. Cerebral Injury in Retrospect. J. Paed. 37:326. Sept.. 1950.
6. Subdural Hematoma in Infants. Pelt & Kahn. J.A.M.A. 98:1851. 1932.
7. Unilateral Paralysis of Diaphragm Due to Phrenic Nerve Injury. Schefreir. Paediatrics. Jan.. 1952.
8. Rupture of Bowel, Including a Case Report of Rupture in Large Intestine with Recovery. Surgery 28:48. July. 1950.
9. Wry Neck. Facial Distortion Prevented by Resection of Fibrosed Sternomastoid in Infancy and Childhood. Brown & McDowell. Annals of Surg. May, 1950.
10. Congenital Muscular Torticollis. Chandler & Altenburg. J.A.M.A. 125:476. 1944.
11. The Use of a Composite Pedicle Graft for Pseudoarthrosis of the Tibia. A. W. Farmer. J.B.J.S. Vol. 34-A No. 3, 1952.

MIND AND MEDICINE

MITSUKO SADA, M.D.*

From the beginnings of medicine, any mental deviation, any "insanity", was looked upon as part of the supernatural influence which good and evil spirits exercise upon man; it was not considered an illness at all. This unwillingness to recognize that a mentally ill person is actually ill continued through the ages, and we find that throughout the history of medicine, the mental patient avoided the doctor, even as the doctor avoided him. But finally, toward the end of the sixteenth century, it was the medical man who maintained his right to care for these unfortunates—to take them out of the hands of the courts, the church, and the philosophers.

Knowledge about the primitive psychiatries is limited, but it is very probable that primitive man lived as a frightened person with his fears embodied in spirits which he felt lived in the world about him. He attempted to get rid of the uncertainty and fear brought on by illness, rather than attempt to eliminate the illness itself. Little change is found in the attitude of the earliest monotheistic nations. The Scriptures report many incidences of mental illnesses, but understanding of mental diseases followed in the tradition of spiritual psychiatry, and in Deuteronomy, the twenty-eighth chapter, is found "The Lord shall smite thee with madness, and blindness, and astonishment of heart." In later centuries mentally ill persons were executed, justification for this being sought in a text from the Bible.

In the Hindu system it was the priests who were absorbed by metaphysics who dealt with the mentally diseased. This is an important point in the future development of medicopsychological ideas. The main trend of Hindu medical psychology was in some ways similar to that of the Greeks, and the Hindu psychology of men was a mystic philosophy as well as psychology. It is the combination of religion and psychology that played such an important part in the history of psychiatry.

Greek science made the first attempt to consider mental illnesses on a scientific medical basis. Greek mythology contained many illustrations of madness, man traditionally becoming mentally ill because the gods took his mind away. But many mentally ill, instead of being considered as sick people, were thought to be able to interpret and cure human ills. Zilboorg thinks that the Pythias of the Delphian oracle, to judge from the description of their behaviour, were afflicted with rather severe mental illnesses. The Greeks, however, were interested in man as a human being and were aware of problems of life, and thus they did not remain absorbed in their mythology. By the sixth century B.C. they had started on their way to observa-

*From a paper delivered to the Osler Society Feb. 26, 1953.

tion and experimentation. The attitude of Greek philosophy of considering the human mind as the domain of religious or secular philosophy had far reaching influence, for even Immanuel Kant at the end of the eighteenth century opposed the medical man's entrance into the field of psychopathology.

The main obstacles to the development of a scientific medical psychology have been supernatural mysticism and abstract philosophy, and these were both present in Greek thought at the time of Hippocrates in the fourth century B.C. However, he boldly introduced psychiatric problems into medicine. In the opening sentences of his *Sacred Disease*, the popular name for epilepsy in those days, he declares, "It thus appears to me to be in no way more divine, nor more sacred than other diseases, but has a natural cause from which it originates like other affections." He made clinical observations on what is now known as "post partum psychoses" and gave a good description of what appears to have been a psychoneurosis with phobias in his *On Epidemics*. However, as far as treatment is concerned, he contributed little. His views on mental diseases were somewhat varied. He sometimes favoured a purely anatomical view which claims that a disease or injury to the brain is the sole cause of mental illness. He also believed in the physiological theory, represented by psychiatric endocrinology to-day, which claims that certain body juices are responsible for madness. He also thought that purely mental or emotional states may produce changes—even physiological changes in an individual. The medical psychology of Hippocrates was, however, chiefly physiological, and he considered phlegm a very important substance (hence a phlegmatic temperament), and especially in mental diseases, yellow and black bile played an important rôle—for example, a sudden flow of bile to the brain causes unpleasant dreams and a feeling of anxiety; an excessive amount of black bile causes melancholia. For centuries Hippocrates remained the only true authority, and for many years no contribution in medical psychology was added to that of Hippocrates.

Aristotle (384–322 B.C.) divided the soul into a rational and irrational part, but the various souls of man were not separable—they act as a unit. Here are the beginnings of the concept of total reactions. Psychological reactions are all total reactions, and Aristotle seems to have understood this. His system of thought was founded during the period of Greece's decline and the Romans' rise as masters of the ancient world.

After the death of Aristotle, progress in many scientific fields was made: Euclid founded his geometry, and Archimedes was contributing to physics. Out of this period came Asclepiades who thought that a mental disease was due to emotional disturbances which he called "passions of sensations". The Greeks considered both delusions and hallucinations under one heading *phantasia*, but Asclepiades considered two varieties. He was able to differentiate between delusions and hallucinations; it was not until the first quarter of the nineteenth century at the time of the psychiatrist Esquirol that such a differentiation was established in psychiatry. He invented devices to make conditions for patients more comfortable, and objected violently to such practices as bleeding, and objected to cells and dungeons in which the mentally ill were kept.

Toward the pre-Christian period, Rome was passing through a phase of humanism in the field of medical psychology. Aretaeus of Cappadocia who lived toward the end of the first century A.D., was the first person known to become interested in what are now labelled as prepsychotic personalities, that is, in the personalities of the individuals who later develop severe mental disease. He abandoned the traditional humoralistic terminology such as phlegmatic, choleric, but turned, instead, to giving clear descriptions. Persons liable to furor or mania, says Aretaeus, are "naturally irritable, violent, easily given to joy, have a facile spirit for pleasantry or childish things." Those prone to depressive tendencies are likely to develop melancholia. This is the first suggestion that some mental diseases are just a psychological extension of a person's normal personality traits.

The Greco-Roman period attained its highest peak in the contribution of Galen (130–200). Seven centuries had intervened between Hippocrates and Galen. Galen assimilated all the medical knowledge which his predecessors had accumulated, added to it his own observations and created a medical system, Galenism, which influenced the medical world almost until the middle of the eighteenth century despite the discovery of the circulation of blood and other discoveries. Galen contributed nothing new to the clinical description or therapy of mental diseases—but the Dark Ages in medical history began with his death in 200 A.D.

The whole field of mental diseases was severed from medicine; it was absorbed by the priest into his system of the supernatural. Hostility to science grew stronger and more open by the beginning of the seventh century. Psychiatry became a study of the ways and means of the devil and his associates. By the ninth or tenth century the psychological problem had become definitely confused with those of theology and theosophy. The human side of psychology was overlooked. The medical man dared not look into normal or abnormal psychology. Those suffering from psychological difficulties were treated as heretics. Psychiatric interests were turned over to the hunter of heretics or to the philosopher who still delved into the nature of the human mind. Psychology and psychiatry became completely isolated toward the close of the twelfth century and were no longer subjects of scientific investigation.

In the thirteenth and early fourteenth century, the general attitude towards mental diseases was not clear. In attempting to solve psychopathological problems, the physician called upon the traditional physiologies of old Greece and Alexandria, and with this were mixed the demonology, astrology, alchemy and prayers of his own day. It was an age of transition, a "prerenaissance of the arts and sciences". The idea that physical illnesses were natural, but that mental illnesses were mostly supernatural became more fixed. Even medicine reflected the general fear which mental diseases aroused, and the mentally sick person became one more to be feared and less to be pitied. Those who were considered authorities confused the heretic and the mentally ill. Astrology and alchemy began to be called *scientiae*, and these sciences were suspected of being of the devil. Thus the magician, the sorcerer, the heretic and mentally ill all began to be looked upon as the servants of the devil. Anxiety over the fear that the devil was about to overrun the Christian world caused both spiritual and tem-

poral powers to unite, and this collaboration was almost complete by the middle of the fifteenth century. Medical psychology became a part of demonology, and the treatment of the mentally ill became largely a problem of legal processes. Thus at the very time that the Renaissance was about to enlighten the world, the darkest period of psychiatry set in. By the end of the fifteenth century, the Christian world was suffering from the effects of superstitions built up through centuries. The physicians were considered to be of no help—the mentally ill were thought to be witches, servants of the demon, and the problems involved were those of salvation of the people and of destruction of the devil's servants. The ravings of the mentally ill appeared sinister, and such individuals might be "possessed" of a devil or be in communion with Lucifer himself. Since Christian theology stressed free will, it was assumed that witches or wizards who had surrendered themselves to the devil had done so of their own accord and consequently deserved the severest of punishment. They were hunted, tortured, and murdered; the standard form of punishment was burning which, it was thought, would deliver the soul. Thus psychiatry continued to be governed by the verse from the twentieth chapter of Leviticus: "a man also, or woman that hath a familiar spirit, or is a wizard, shall surely be put to death: they shall stone them with stones: their blood shall be upon them."

Two German Dominican monks led a movement to exterminate witches. It was to them a religious mission. The two, Sprenger and Kraemer, wrote a book *Malleus Maleficarum*—the Witches' Hammer, which was published about 1487 or 1489. It consisted of three parts, the first part setting out to prove the existence of witchcraft and witches, and even suggesting that it was heresy not to believe in witches. It included descriptions of various types of witches, and the different methods for their identification, and described as well, the legal forms of examining and sentencing a witch.

At the beginning of the sixteenth century, the attitude of the medical man remained conservative on the question of witchcraft. In medical matters the authority of Galen remained, just as the dogma of the church prevailed in other fields. Towards the middle of the sixteenth century, however, scepticism began to rise with a growing protest against demonological psychiatry. The man who made the greatest contribution to psychiatry during the Renaissance was Johann Weyer (1515–1588). He could not, of course, tackle the problem of mental disease without dealing with demonology and the Inquisition. In his book *De Praestigiis Daemonum* he tries to establish the fact that there are evil people who resort to poisons to do harm to their enemies, that these are criminals and should be punished. These, however, are not to be confused with most of the witches who are innocent but sick people who should be taken to a physician for treatment. In summarizing Weyer's contribution, it can be said that he was the first medical man whose major interest was in mental diseases and thus presaged the formation of psychiatry as a medical speciality. He was a clinical and descriptive psychiatrist whose work inspired the development of an observational branch of medicine which helped to formulate the descriptive system of psychiatry of the end of the nineteenth century. As Zilboorg states, "Psychiatry had to liberate the sick from the thorns

and tentacles of political prejudice, theological tradition, and legal intricacy . . . . It was Weyer who started the process with relentless conviction, boundless compassion, and great effectiveness."

The seventeenth century, and a great part of the eighteenth century, presented a striking paradox—the scientist and physician became so engrossed with nature and man that study of the human mind was left to the theologians and to the increasing numbers of layman philosophers. The influence of the Inquisition was on the wane, and the church did not have so strong a control over scientific thought. The medical thinker of the seventeenth century did make a contribution in studying the human body in seeking out the cause of mental illness. But psychiatry on the whole was surrendered to the nonphysician, the philosopher, and men like Francis Bacon, Descartes, Hobbes, Locke and Spinoza were the ones concerned about how the mind, will and emotions work and influence man's actions. None of these were physicians except John Locke. None of them could contribute much toward the understanding of mental disease.

In the field of mental diseases, the medicine of the seventeenth century wavered between organicism and humanitarianism. The strict organicist, interested mainly in anatomy and physiology, worked in his dissecting room, leaving the humanitarian aspects of the disease to take care of themselves. The humanitarian was surrounded by problems of social conflicts and thus could not give more attention to the psychological problems of his patients. The correlation of psychiatry with sociology was left for the physicians of the nineteenth century to effect. Even the philosophical psychology of the seventeenth century was an advance, for it was a descriptive analysis of mental functions, and helped to draw medical psychology away from theology. Although mental diseases were classified according to their clinical manifestations, they were still attributed to faulty functioning of body juices in the blood and the brain, or the fluid flowing through the nerves. Thus the treatment of mental diseases in this century was characterized not only by therapeutic blood letting, but also by blood transfusions. Zilboorg's comment on this is, "Little would Harvey have suspected that his great discovery would be put to such rather naïve use by the medical man whose eagerness to cure a mental disease always surpassed his understanding of the underlying psychological processes."

By the time of the eighteenth century, medicine had rescued mental disease from the sadism of a superstitious world, and mental illness came to be regarded as the misfortune of man as a person, and the lunatic became the object of concern as any sick man. The clinical approach and treatment of the mentally ill, however, remained the same. Johann Christian Reil (1759–1813), a great advocate of psychological treatment of the mentally sick still advised what he called "noninjurious torture". He thought that throwing patients into water, and firing cannons in order to bring them to their senses were rational and legitimate methods of treatment. It was even useful to arouse anger, disgust and pain in certain cases. Psychology, as has been pointed out, was now in the hands of the philosopher, and toward the end of the eighteenth century, the philosopher was claiming psychopathology also as his domain. Im-

manuel Kant insisted that the expert psychiatric witness in criminal cases regarding any question of insanity should not be from the medical faculty, but from the faculty of philosophy. In spite of this, the effort of medicine to win the field of mental diseases continued. The effort separated into two directions which, however, often converged. One was the development of clinical observations and their systematization; the other was the reform of the care of the mentally sick, which led to the establishment of hospitals for mental diseases. Literature on the subject of mental diseases was poured out—an indication that psychiatry as a specialty had started.

Toward the close of the eighteenth century, man as an individual was being left to the public-minded citizen; the neglect of man by the scientific psychiatrist was becoming more real. In the case of the insane, these unfortunate individuals had long been neglected and abused before the new humanitarianism uncovered their plight. John Howard of England was shocked by the treatment of both the sane and the insane in hospitals and jails, and it was his efforts that did much to promote improvements during the late eighteenth century.

The blend of humanitarianism and scientific extension was most advanced in France, and so it was the French doctor who became the most representative worker for the new psychiatric system. From this new era came Joseph Daquin (1733–1815) who stated a truth that had, until now, been overlooked: a hospital for mental diseases is primarily an institution for treatment, and furthermore, a place of research—thus, only in a hospital can be found enough clinical material with which to teach psychiatry and to make new investigations. Phillipe Pinel (1745–1826), the great French advocate of "moral treatment" of the mentally ill, studied psychiatric problems in the mental asylums, and soon found that brutal treatment did not check the ravings of the ill, but indeed actually promoted them. Kindness led to better results. Thus humanitarianism contributed to therapeutic procedures. In 1792, Pinel was placed in charge of the Bicêtre, a hospital for insane men. His success in striking off the chains in this asylum, and later at the Salpêtrière hospital for women, together with his psychiatric writings, did much to arouse interest in his "moral treatment" throughout the western world. Although such instruction was not official, he gave talks to medical students while on ward rounds, and thus started clinical teaching in psychiatry. He was a founder of a psychiatric dynasty "both benevolent and enlightened". By the middle of the nineteenth century, the combined efforts of the early psychiatrists in France resulted in the passing of a law which placed mental institutions under supervision of the central government with regulation of the transportation, admission and discharge of patients. The hospitals were then placed under medical directors instead of just wardens. All this contributed toward making psychiatry a medical specialty in which the physician could find a career.

Conditions in English mental asylums in the eighteenth century were bad, and the three major institutions—Hanwell, St. Luke's, and Bethlehem (known as Bedlam)—were in an appalling state. In Bedlam, which had been founded in the thirteenth century, patients were shown to visitors who paid for this form of amusement. In England, William Tuke accomplished something similar to

Pinel by founding, in 1796, and administering the York Retreat. He was not a physician, but a merchant, and a member of the Society of Friends. Here, mental patients were treated as kindly as sick human beings. It was shown that there was no necessity for dark cellars and brutal restraint in the handling of such patients. York Retreat was a shining example, and it was visited every year by physicians from Europe and America. It had an influence especially on American care of the mentally ill.

The middle of the nineteenth century saw an incredible increase in activities in the field of mental disease. Within twelve years, seven psychiatric journals were founded in five countries—France, Germany, America, England and Holland. The growing interest in the mentally ill, the study of mental illness, the building of hospitals and clinics, and the foundation of psychiatric societies and psychiatric periodicals made the psychiatry of the nineteenth century one with many confusing aspects.

The nineteenth century had a great record for the hospitals opened for the mentally ill. Here our attention is turned to America and Dorothea Lynde Dix (1802–1887). This outstanding woman, a retired school teacher, became interested in the conditions of jails and almshouses and spent several years investigating the institutions, especially the treatment of the pauper insane. Her report to the state legislature dealing with the abuses that she had discovered resulted in more adequate care and treatment of the insane. She extended her work to many states, her labours resulting in the establishment of insane asylums in twenty states and in Nova Scotia and Newfoundland. The history of medical psychology in America during the nineteenth century includes the history of the American Psychiatric Association which was formed in 1844. Thirteen superintendents of hospitals for the insane met to discuss their problems; they founded the Journal of Insanity, also in 1844. In the general course of psychiatric thought, however, the leadership still belonged to England and continental Europe.

As the nineteenth century was about to end, it was ready to revive the study of man as man and not as a nameless entity in society. Such was the setting as Sigmund Freud (1856–1939) entered the stage of medical psychology. Freud turned to hypnotism, but he used it only so that the patient could speak spontaneously and free himself of the emotions connected with the memories which the patient was describing while hypnotized. This was known as the "cathartic method". This was the discovery of the unconscious. It was made on a neurotic patient, not a psychotic. This was the first time in the history of medical psychology that the cause of an illness had been discovered through a therapeutic agent's attempt to remove the cause. In this new method of free association, the patient was allowed to talk at random. The method of analysing and interpreting what the patient said and did was called psychoanalysis. Freud's concept of man was that of total personality. His great contribution was the descriptive method of subjective psychological states by allowing the patients to reveal their own subjective states. In other words, he introduced the objective method of the study of the subjective conscious and unconscious state of the patients. Thus within Freud's lifetime the whole field of psychopathology was revolutionized, for psychiatry, whether

it approved psychoanalysis or not, had to recognize the new facts. The significance has been aptly worded thus: "The witch was not fully freed from contempt and suspicion until the revolution wrought by psychoanalysis set her free."

We can see that throughout the ages psychiatry has not been able to keep up with medicine, but this is understandable, for medicine in its restricted sense had a criterion of illness in pain and other forms of physical suffering familiar to both doctor and patient. Psychiatry did not. The whole history of medical psychology is marked by the medical man's struggle against the prejudices of the ages. Psychiatry advanced most when humanism and respect for the individual was marked. In spite of our past prejudices, and in spite of mistaken concepts in psychology, psychiatry to-day has developed into a special branch of the art of healing, and a greater understanding of mental illness has been reached.

BIBLIOGRAPHY

Zilboorg, Gregory: Mind, Medicine and Man, Harcourt Brace and Company, New York, 1943.

American Psychiatric Association: One Hundred Years of American Psychiatry, Columbia University Press, N.Y., 1944.

Zilboorg, G., and Henry, George: A History of Medical Psychology, W. W. Norton and Co., Inc., N.Y., 1941.

Whitwell, J. R.: Historical Notes on Psychiatry, H. K. Lewis and Co. Limited, London, 1936.

Adhesions are the refuge of the diagnostically destitute.—Osler.

ABSTRACTS

Treatment of Staphylococcic Infections with Erythromycin: Kirby, Forland and Maple . . . Archives of Internal Med., vol. 92, no. 4, 1953, pp. 464–470.

From the standpoint of antibiotic therapy, infections caused by staphylococci constitute one of the major problems at the present time. In hospitalized patients approximately 70% of staphylococcic infections are caused by penicillin-resistant organisms and 40 to 60% are resistant to aureomycin) and oxytetracycline. In many instances, the only antibiotics available for treatment are bacitracine and chloramphenicol, both of which must be administered with caution because of possible toxic reactions.

Thirty-four patients with infections caused by antibiotic-resistant Staph. Aureus were treated with erythromycin. Evaluation was difficult in many cases, because other therapeutic measures were carried out simultaneously. In general, however, the response appeared comparable to that observed with penicillin in infections caused by penicillin-sensitive staphylococci.

Initial improvement occurred in 23 patients with soft tissue infections. In 17 the infection was eradicated within two weeks, and periods up to two months were required for healing in 3 others. In three patients relapses occurred when treatment was stopped. Of 10 patients with chronic osteomyelitis, only 1 failed to respond to erythromycin therapy. Acute flare-ups were readily controlled when they occurred, and the chronic infection was arrested or eradicated in eight patients following saucerization of bone and removal of devitalized tissues. In two patients, one with staphylococcic pneumonia secondary to pneumococcic pneumonia and the other with peritonitis, cultures became overgrown with Proteus vulgaris and in one this organism was cultured from the blood stream. The patient with peritonitis eventually recovered and the one with pneumonia died with multiple staphylococcic abscesses throughout his body.

Prior to therapy, all 34 strains of staphylococci were highly sensitive to erythromycin and were resistant to penicillin, aureomycin and oxytetracycline. In one patient with chronic osteomyelitis of the spine erythromycin-resistant organisms developed after 6 weeks of therapy.

However, in three patients with soft tissue infections the organisms remained sensitive after three weeks of therapy. In the other cases follow-up sensitivity tests were not possible, because the cultures became negative. Erythromycin was well tolerated by the oral route and virtually no side reactions were encountered. Serum concentrations of the antibiotic were remarkably high and well sustained.

D. E. Boyer

Penicillin Reactions: Their Nature, Growing Importance, Recognition, Management and Prevention: R. A. Kern, M.D.? N. A. Wimberley, Maj. M. C. a.j. med. sciences: Vol. 226, No. 4, 1953 . . . pp. 357–375.

This original article covers, in a most thorough manner the features of penicillin reactions from all aspects. In summary, these are:

1. Penicillin is the commonest cause of drug allergy.
2. Manifestations of penicillin sensitivity cover almost the whole gamut of allergic reactions and immunological mechanisms.
3. The severest is that incident to anaphylactic sensitivity, and its greatest danger lies in death from anaphylactic shock.
4. Exfoliative dermatitis and severe irreversible vascular reactions, possibly going on to periarteritis nodoasa, contribute additional allergic deaths.
5. Individuals with a personal or familial history of allergy are more easily sensi-

tized to penicillin, and furnish the majority of severe and fatal penicillin sensitivities.

6. Much penicillin sensitivity is unnecessary, and preventable by not giving penicillin in minor ailments, avoiding local applications of the drug, avoiding preparations of depot penicillin unless they are decidedly necessary, giving preference to the oral route of administration, and avoiding combined parenteral injections with other possible antigens.

7. The most dangerous type of penicillin sensitivity, anaphylaxis, can be usually recognized by skin test, especially by the immediate whealing reaction on cutaneous or intracutaneous testing, and at times in lesser degrees of sensitivity, also by the delayed (24 to 48 hour) intracutaneous reaction.

8. Penicillin reactions may be largely avoided by careful attention to an allergic history in the patient's background, by questioning with regard to previous penicillin therapy and reactions, and by proper precautions in the management of such patients.

9. The oral route of penicillin administration should be preferred to parenteral routes.

10. If parenteral administration is necessary, the injection should be into the arm only, and at a low enough level so that it will not prevent the effective use of a tourniquet in case of severe reaction.

11. The treatment of th several types of penicillin reactions is presented. Emphasis lies in preparedness to meet the emergency of anaphylactic shock.

D. E. Boyer

Cerebral Edema and its Relation to Barbituric Acid Poisoning. L. H. Mousel, M.D., J.A.M.A., vol. 153, no. 5, pp. 459–462.

It is believed that the earliest change in the anoxic brain is cerebral edema. If it persists, then by purely mechanical means oxygen will be denied rapid access to the cell, so that the anoxia becomes worse, and a vicious circle is established that leads to cellular death. On the supposition that cerebral edema is probably responsible for the severe complications frequently seen in barbiturate poisoning, Dr. Mousel reports three cases of severe barbiturate intoxication treated with 25% salt-poor human serum albumen.

The recovery phase in all three patients was similar. In cases 1 and 3 return of reflexes occurred 23 and 17 hours respectively after serum albumen was given. Return of reflexes occurred eight hours after serum albumen was given in case 2. All of the patients showed signs of voluntary activity and return of consciousness within a few hours after return of deep reflexes. There were no maniacal tendencies and restraints were not required. This is in sharp contrast to the behaviour of many patients recovering from barbiturate poisoning when the usual therapeutic agents are used.

Definite conclusions cannot be made from the study of three cases; however the response to, and results of, the treatment were so uniform that further study seems warranted. The author believes that analeptics should be abandoned in the treatment of barbiturate intoxication. Treatment should be directing toward correcting the cerebral anoxia by eliminating cerebral edema through the use of salt-poor serum albumen or some other agent that will accomplish the same result by action of its high osmotic pressure in drawing the intracellular fluid back into circulation. General supportive measures such as adequate oxygen and fluid therapy are essential.

D. E. Boyer,
IV Meds.

Isoniazid: Lancet, 263:869-870, 1952.

The earliest effects of this drug on the tubercle bacillus have been found to be quite powerful, but the conclusion reached in the Lancet editorial after a study of the reports of two British investigating committees, was that isoniazid cannot yet be recommended for use alone in the treatment of pulmonary tuberculosis.

The investigations evaluated the drug from the following aspects: chemotherapeutic clinical tests, pharmacologic, and

bacteriologic investigation of the drug.

For the first study, made under the auspices of the Medical Research Council, 331 patients with different degrees of pulmonary tuberculosis were divided into two groups. One group, of 173 patients, received isoniazid alone; the 158 patients were given streptomycin and PAS. After three months of treatment, the isoniazid-treated group showed an average weight gain of 11 lb., compared to 6 lb. for the streptomycin-PAS patients. This difference is considered significant, yet both groups responded similarly as judged by general condition, sedimentation rate, temperature changes, and radiologic appearances.

The second study was conducted at Guy's Hospital. The patients all had chronic tuberculosis. Clinical evaluation, sedimentation rate, and weight were the criteria assessed. Sputum specimens from such patients were studied twelve times each month.

Isoniazid alone, even in the rather low doses used, produced in the first four or five weeks a pronounced improvement in most cases. However, the effect on the sputa was only temporary. Some cases were already relapsing by the fifth week and isoniazid-resistant strains were cultured from the sputa. Most of the patients gained weight until about the twelfth week. Thereafter the weight remained stationary and the clinical condition began to deteriorate.

Laboratory studies of isoniazid at Guy's Hospital yielded the following conclusions:

1. Isoniazid alone will inhibit corneal tubercle development in mice inoculated intracorneally with Mycobacterium tuberculosis. But the lesions appear after the usual interval when the drug is discontinued. With streptomycin dosage alone, the disease is almost entirely prevented, though occasional lesions develop even during treatment. When therapy is discontinued, lesions rarely develop later in the streptomycin-treated mice.

A combination of isoniazid and streptomycin is much more efficient in the mice. No lesions develop either during or after treatment. A combination of PAS and isoniazid is no more effective than isoniazid alone.

2. In liquid medium, sensitivity of the micro-organism to isoniazid depends on length of time of incubation of culture. A standard period of incubation is necessary. When the sensitivity is read after fourteen days or less of incubation, growth is found to be inhibited by an isoniazid concentration of 1 part in 100 million; in older cultures, growth is not inhibited with concentrations 600 times greater.

3. The action of isoniazid in vitro is profoundly modified by small changes in temperature—a rise from 37 to 40 C. increases the bactericidal action of isoniazid. This may explain the dramatic effect the drug exerts on toxic patients with high fever.

4. Isoniazid-resistant strains of M. Tuberculosis are quickly and easily produced in vitro.

F. P. Ceresney

Present Status and Future Possibilities of a Vaccine for the Control of Poliomyelitis: A. Sabin, M.D., Cincinnati; A.M.A., Diseases of Children; vol. 86/3; pp. 301–310, 1953.

The author commences his article with the statement that "such a vaccine is not now at hand and that one can only guess as to what is around the corner."

The objective is to provide immunity for mankind without the risk of paralysis which is attendant in the incurring of a natural, acquired immunity. The problems were immunological; how many different types of polio virus were there; how could more living laboratory material be easily obtained; how about the danger of post-vaccinal paralytic accidents occurring.

Several of the recent acquisitions to polio information are noted:

1. There are over 200 strains of moderate or high virulence found in various parts of the world; that there were only three major immunological types. These studies also revealed that the Type 1 (Brunhilde-like) strains were most regularly

responsible for the major epidemics, while the Type 3 (Leon-like) strains were encountered only irregularly during epidemics. The Type 2 (Lansing-like) strains thus far have not been found to be the cause of a single epidemic, although they have been recovered in sporadic cases of paralytic and nonparalytic poliomyelitis, and the vast majority of adults, the world over, have antibodies for this type of virus.

2. It has been demonstrated by Enders, Weller and Robbins, that the polio viruses not only multiply in human embryonic and adult non-nerve tissues in vitro, but also produce a cytopathogenic change by which the presence of virus can be recognized without having to resort to animal inoculation. Bodian has shown that the amount of passively introduced antibody required to protect cynomolgus monkeys against paralytic infection by the intramuscular or oral routes is very much smaller than that needed to protect against infection by the nasal or cerebral routes. Freund's studies indicated that certain adjuvants can enhance the immune response to a variety of antigens, including those of poliomyelitis viruses.

The field trials of Hammon and his associates on the prophylactic effect of small doses of human gamma globulin, if confirmed by future observations, also suggest that the amount of antibody required to protect human beings against the paralytic consequences of poliomyelitis infection may not be very large.

With this new information there are three main approaches to the problem of immunization against poliomyelitis: (1) a "killed" virus vaccine, (2) immunization with active virus under cover of antibody, and (3) an avirulent virus vaccine. The author discusses some of the fundamental concepts connected with these three approaches, and in closing reminds his readers that though there is as yet no practicable vaccine for the control of poliomyelitis and that many more workers in this field are needed, the recent clinical and laboratory findings indicate better methods of prophylaxis are soon forthcoming.

F. P. Ceresney

NEWS AND NOTES

The following awards have been made from the G. Roy Sproat and Katherine Sproat Bursary Fund: I. Gallish, First Medical Year, an award of $200, and C. L. Berlie, Third Medical Year, also an award of $200.

* * *

The Phi Delta Epsilon Medical Fraternity Lecture was given on November 16 by Dr. Burrill B. Crohn. His subject was "Crohn's Disease."

* * *

Recent visitors to the medical school have included Dean Mangalik of St. George's Medical College, Lucknow, India; Dean Govind Lal Sharma of the Medical College and Hospital, Nagpur, India; Dean Niilo Pesonen of the Medical Faculty and Vice-President of the University of Helsinki, Helsinki, Finland; Dean S. Sutherland of the Faculty of Medicine, University of Melbourne, Melbourne, Australia.

* * *

New members elected to A.O.A. for 1953–54 are J. D. T. Ainslie, R. M. Ehrlich, G. S. Cohen, Mrs. M. L. Cohen of the class of 5T5 and F. E. A. Griffith, J. G. Humphrey, A. N. Lofchy, N. W. Mortimer, R. L. Perkin, E. A. Silverstein, R. J. Watson of the class of 5T4.

* * *

The Canadian Life Insurance Association has given a number of grants to the University of Toronto for medical research. Projects which will benefit from these grants are:

1. Studies of the process of ageing being carried on by the Banting and Best Department of Medical Research.

2. A study of severe malnutrition in infancy and childhood under the direction of Dr. H. W. Bain of the Hospital for Sick Children.

3. Laryngo-Tracheo-Bronchitis — being studied at the Hospital for Sick Children by Drs. E. A. Morgan and A. J. Rhodes.

4. A study of extra-corporeal circulation directed by Dr. W. T. Mustard with the object of developing a substitute for the heart during cardiac surgery.

NOTICE

Dr. Stephen Rudnai, who was listed in the previous issue as address unknown, has sent his present address to us. He may be reached at

Calgary General Hospital,
Calgary, Alberta.

excellent bacteriostatic and
bacteriocidal activity against
a wide variety of vaginal pathogens

Triple Sulfa Cream

• hastens healing • relieves symptoms • eliminates discharge

—following conization and vaginal plastics

—following cervical cauterization

—in routine postpartum care

Dosage: one applicatorful intravaginally twice daily for one week. With improvement, reduce to single application daily.

On original prescriptions specify "Triple Sulfa Cream *with applicator.*"

Also available—*"tube only"* refills.

Ortho

BETTER WOMANHEALTH
THROUGH RESEARCH

Active Ingredients: sulfathiazole, N'acetyl-sulfanilamide, N'benzoylsulfanilamide and urea peroxide in a water-dispersible, absarbable cream base.

A PAGE FROM THE "Frosst" ALBUM

"OSTOFORTE" COMPOUND

Treatment of chronic arthritis with massive doses of vitamin D, while entirely empirical, has proved beneficial in a great number of cases. Where the patient's diet is restricted, or appetite diminished, Ostoforte Compound capsules provide not only massive doses of D, but also adequate amounts of other essential vitamins.

Where the diet is adequate in vitamins B, C and A:

"OSTOFORTE"
Capsule No. 651 "Frosst"
Each capsule contains 50,000 I.U. Vitamin D

Complete therapeutic information on request.

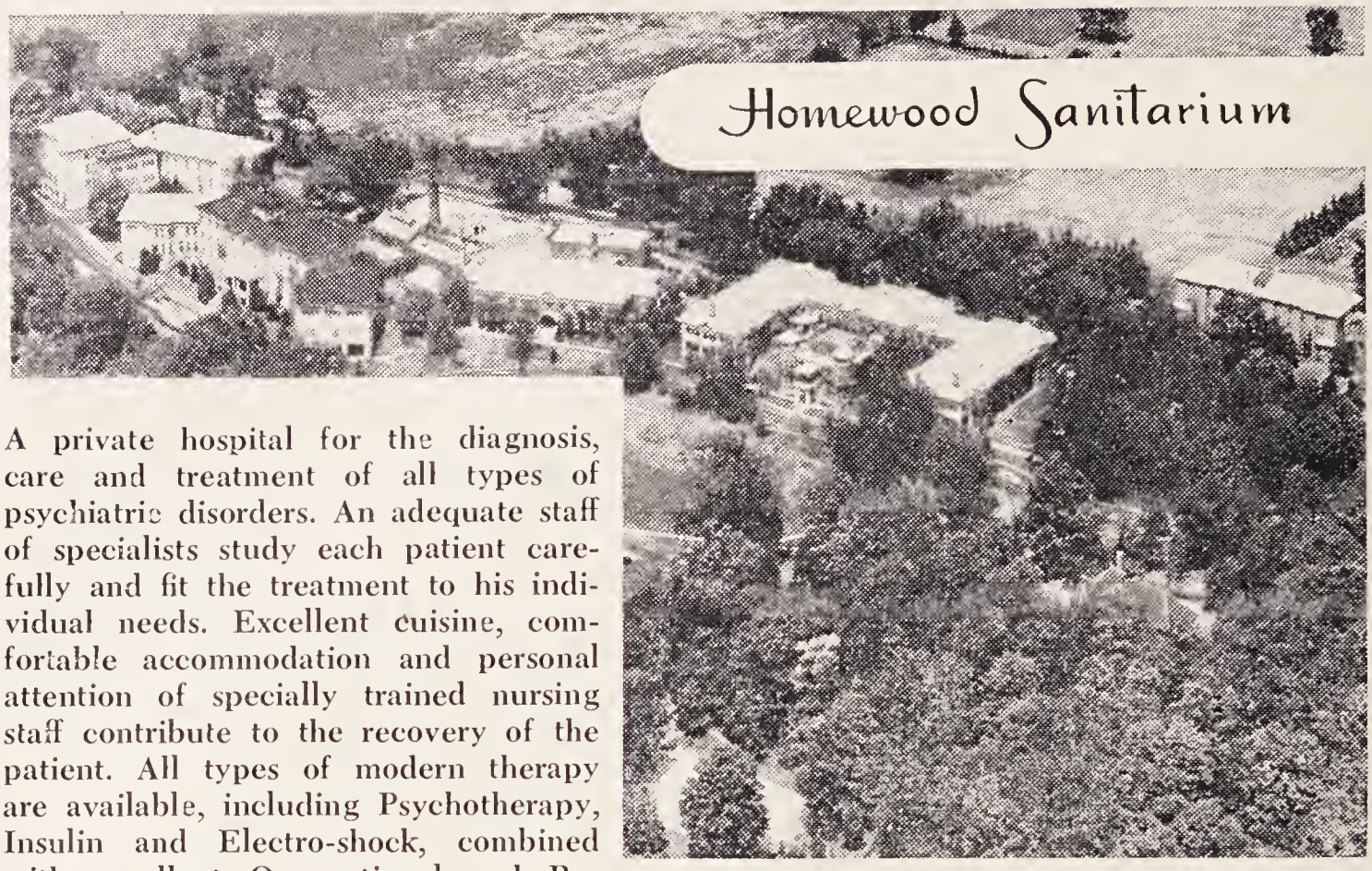
Charles E. Frosst & Co.
MONTREAL CANADA

"OSTOFORTE" COMPOUND
Capsule No. 671 "Frosst"

Ingredients	in each capsule	in averoge daily dose (4 capsules)
Vitomin D.....	50,000 I.U.	200,000 I.U.
Vitomin A.....	1,666 I.U.	6,664 I.U.
Thiamine hydrochloride	0.67 mg.	2.67 mg.
Riboflovin.....	1.0 mg.	4. 0 mg.
Niacinamide.....	6.67 mg.	26.67 mg.
Ascorbic acid.....	15.0 mg.	60.0 mg.

DOSE: Up to six capsules daily.
MODES OF ISSUE: Boxes of 50 and 100.

IMPORTANT: Ostoforte Compound or Ostoforte should not be administered to patients with "impaired kidney function" nor to children in repeated doses.



A private hospital for the diagnosis, care and treatment of all types of psychiatric disorders. An adequate staff of specialists study each patient carefully and fit the treatment to his individual needs. Excellent cuisine, comfortable accommodation and personal attention of specially trained nursing staff contribute to the recovery of the patient. All types of modern therapy are available, including Psychotherapy, Insulin and Electro-shock, combined with excellent Occupational and Recreational facilities.

The Sanitarium buildings, accommodating 225 patients, are situated in a very attractive setting within the confines of the City of Guelph. Visits by physicians and other interested parties are always welcomed. For further information write or telephone (Guelph 53).

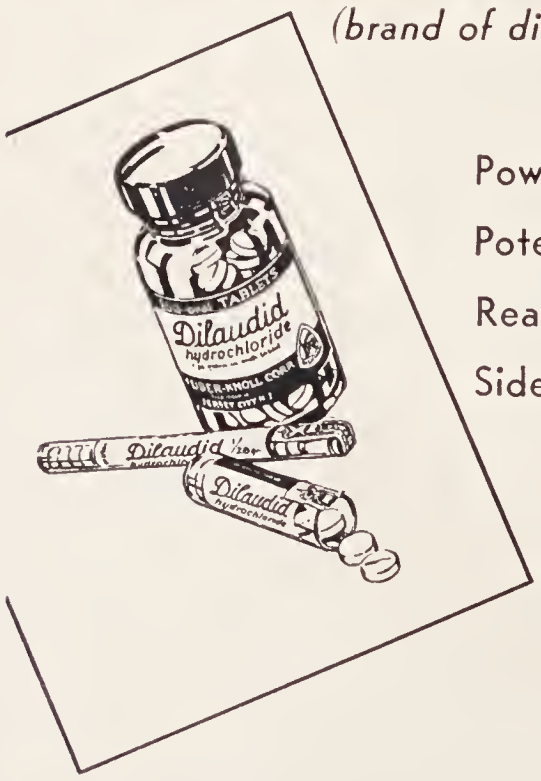
A. L. MacKINNON, M.B.,
Medical Supt.

THE HOMEWOOD SANITARIUM OF GUELPH, ONTARIO, LIMITED

Dilaudid hydrochloride

(brand of dihydromorphinone hydrochloride)

COUNCIL ACCEPTED



Powerful opiate analgesic - dose, 1/32 grain to 1/20 grain.

Potent cough sedative - dose, 1/128 grain to 1/64 grain.

Readily soluble, quick acting.

Side effects, such as nausea and constipation, seem less likely to occur.

An opiate, has addictive properties.

Dependable for relief of pain and cough, not administered for hypnosis.

● Dilaudid, T. M. Reg. Canada

Product of Bilhuber Knoll Corp., Orange, N. J.

MERCK & CO. Ltd. Selling Agents **MONTREAL**

Riches from Rice Bran...

"Until the clinical values of pantothenic acid, pyridoxine, choline, biotin and the other factors in the B group have been demonstrated, it is urged that vitamin B complex preparations be selected on the basis of the cost of **thiamine, riboflavin** and **nicotinic acid** in the **1:2:10 ratio.**" *

THE B•PLEX FORMULA

Each ml. (cc.) provides

√ Thiamine	.125 mg.
√ Riboflavin	.250 mg.
√ Niacin	1.250 mg.
*Pyridoxine	.125 mg.
*d-Pantothenic Acid	.625 mg.
*Biotin	.001 mg.

*The significance of these vitamins in human nutrition is not yet established.

SUGGESTED DOSE: 8 cc. to 24 cc. (approximately 2 to 6 teaspoonfuls) daily as directed by the physician.

from natural rice bran source . . .
. . . plus added B factors

B•PLEX

Wyeth
Registered Trade Mark

ELIXIR VITAMIN B COMPLEX

Also available: B•PLEX CAPSULES
B•PLEX INJECTION

*Vitamin Therapy in General Practice: Edgar S. Gordon, M.D., M.A. and Elmer L. Sevringhaus, M.D., F.A.C.P.

for simple, effective
control
without a diaphragm

with measured-dose
applicator

Ortho

* TRADE-MARK REGISTERED

Pharmacy...

AN ANCIENT AND HONORABLE PROFESSION

A drugstore 1652, with garden for medicinal herbs. From pharmacopoea of Valerius Corducs, Antwerp. (The Bettman Archive.)

Yesterday and to-day it's best to

LET THE PHARMACIST DO *ALL* YOUR DISPENSING

Doctor — your time is much too valuable for financing and running a private dispensary. The time spent tending stock and making and renewing prescriptions can well be devoted to more useful and more satisfying pursuits. Make full use of your pharmacist — a professional man, skilled in all things pharmaceutical.

THE ONTARIO RETAIL PHARMACISTS' ASSOCIATION

ONTARIO RETAIL PHARMACISTS ASSOCIATION

"PINOCODEINE"

Cough Sedative

Results have proved the effectiveness of Pinocodeine in the treatment of acute and chronic coughs, bronchitis and similar affections of the respiratory tract. It does not diminish the appetite, disturb the stomach nor constipate.

"PINOCODEINE"

Each fluid ounce contains:

Pinus strobus	32 gr. (2.1 G.)
Prunus virginiana	32 gr. (2.1 G.)
Sanguinaria canadensis	4 gr. (0.25 G.)
Populus balsamifera	2 gr. (0.12 G.)
Chloroformum	1 min. (0.6 cc.)
Codeinae phosphas	1 gr. (65 mg.)

DOSE: One to two drams every 4 hours.

MODE OF ISSUE: 16 fluid ounce bottles.

Pinocodeine readily lends itself to modification as indications demand:

Early Bronchitis:

℞ Potassium citrate	6 dr.
Tinct. of ipecac	4 dr.
Pinocodeine q.s. ad	6 oz.

Bronchitis:

℞ Ammonium chloride	4 dr.
Pinocodeine q.s. ad	6 oz.

To Abort a Cold:

℞ Atropine sulphate	1/16 gr.
Pinocodeine q.s. ad	6 oz.

DOSE: One to two drams, for all formulae.

Frosst — Since 1899 — The Symbol of Progress in Pharmaceutical Research

Charles E. Frosst & Co.

MONTREAL, CANADA

"FARMER'S WIFE"

3 FORMULA MILKS

1 **WHOLE MILK**
Butterfat 8%
Calories 45 per oz.

2 **PARTLY SKIMMED MILK**
Butterfat 4%
Calories 32 per oz.

3 **SKIMMED MILK**
Butterfat 2%
Calories 29 per oz.

All "Farmer's Wife" milks are Vitamin D increased to 480 International Units per pint by the addition of pure crystalline Vitamin D_3.

Please write for professional information

COW & GATE
(CANADA) LIMITED
GANANOQUE, ONTARIO

1-3

for refreshing sleep – and a fresh awakening

CARBRITAL®

Calms the restless . . . rests the sleepless

Administered at bedtime, CARBRITAL acts promptly to induce sound, refreshing sleep. Patients relax easily, sleep restfully, and awaken fresh and alert. In patients troubled by daytime tension or anxiety, CARBRITAL promotes relaxation and tranquility.

Available in Kapseals,® or as an Elixir for easily individualized dosage, CARBRITAL is valuable in a wide range of indications including insomnia, nervous tension, and preoperative or obstetrical preparation.

Each CARBRITAL KAPSEAL (Full-strength) contains:	
Pentobarbital sodium	1½ grains
Carbromal	4 grains
Each CARBRITAL KAPSEAL (Half-strength) contains:	
Pentobarbital sodium	¾ grains
Carbromal	2 grains
Each fluidounce of CARBRITAL ELIXIR contains:	
Pentobarbital sodium	2 grains
Carbromal	6 grains

CARBRITAL KAPSEALS, full- or half-strength, may be taken by adults in doses of one or more, on schedules determined by the physician. Children may be given ½ to 1 teaspoonful of CARBRITAL ELIXIR; adults 1 to 2 teaspoonfuls or more as required.

MEDICAMENTA FERMENTA P D & CO.

Parke, Davis & Company, Ltd.

WALKERVILLE, ONTARIO